National Registration Authority
For Agricultural & Veterinary Chemicals

First Floor, Industry House, National Circuit, Barton ACT

PO Box 240. Queen Victoria Terrace. Parkes ACT 2600
Australia

Tel: (06) 272 5158 Fax: (06) 272 4753

Public Release Summary

HALOSULFURON-METHYL

In The Product

SEMPRA HERBICIDE BY MONSANTO

1994

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This document is published by the
National Registration Authority for
Agricultural and Veterinary Chemicals.

For further information, please contact:

Dr Ronald Eichner
National Registration Authority
PO Box 240
Queen Victoria Terrace
PARKES ACT 2600

Ph: (06) 2725248
Fax: (06) 2723218

FOREWORD

The National Registration Authority for Agricultural and Veterinary Chemicals (NRA) is an independent Statutory Authority with responsibility for the assessment and approval of agricultural and veterinary chemical products prior to sale and use in Australia.

In undertaking this task, the NRA works' in close cooperation with advisory agencies including the Department of Human Services and Health (Chemical Safety Unit), the Environment Protection Agency (EPA), the National Occupational Health and Safety Commission (Worksafe Australia) and State Departments of Agriculture and Health.

The NRA has a policy of encouraging openness and transparency in its activities and seeking community involvement in decision making. The publication of Public Release Summaries for all products containing new active ingredients is a part of that process.

The information and technical data required by the NRA in order to assess the safety of new chemical products and the methods of assessment must be undertaken according to accepted scientific principles. Details are outlined in the document "Interim Requirements for the Registration of Agricultural and Veterinary Chemical Products" which can be obtained from the NRA.

This Public Release Summary is intended as a brief overview of the assessment that has been completed by the NRA and advisory agencies. The document has been deliberately presented in a manner that is likely to be informative to the widest possible audience thereby encouraging public comment. Further more detailed technical assessment reports on occupational health and safety aspects, public health considerations and environmental impact are available from the NRA on request.

As a relatively new organisation, the NRA would welcome comment on the usefulness of this document and suggestions for further improvement. Comments should be forwarded to The National Registration Manager, National Registration Authority for Agricultural and Veterinary Chemicals, PO Box 240, Queen Victoria Terrace, Parkes, ACT, 2600

ABBREVIATIONS AND ACRONYMS WHICH MAY BE USED IN THIS DOCUMENT

ADI	Acceptable Daily Intake (for humans)
CSU	Chemical Safety Unit (of the Department of Human Services and Health)
d	Day
EC50	Concentration at which 50% of the test population of fish are immobilised
EUP	End Use Product
Fo	Original Parent Generation
h	Hour
ha	Hectare
HPLC	High Performance Liquid Chromatography
id	Intradermal
ip	Intraperitoneal
im	Intramuscular
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
L	Litre
LC50	Concentration that kills 50% of the test population organismsk
LD50	Dosage of chemical that kills 50% of the test population of organisms
m	Metre
mg	Milligram
mL	Millilitre
MRL	Maximum Residue Limit (a legal limit)
MSDS	Material Safety Data Sheet
ng	Nanogram
NHMRC	National Health and Medical Research Council
NOEC/NOEL	No Observable Effect Concentration/Level
NRA	National Registration Authority for Agricultural and Veterinary Chemicals
po	Oral
ppb	parts per billion
ppm	parts per million
s	Second
sc	Subcutaneous

SUSDP	Standard for the Uniform Scheduling of Drugs and Poisons
T-Value	A value used to determine the First Aid Instructions for chemical products that contain two or more poisons
TGAC	Technical Grade Active Constituent
WDG	Water Dispersible Granule
WHP	Withholding Period

EXECUTIVE SUMMARY

Introduction

The purpose of this document is to provide a summary of the data reviewed and an outline of regulatory considerations for the proposed clearance and registration of the chemical halosulfuron-methyl in the product SEMPRA HERBICIDE BY MONSANTO as a herbicide for the selective post-emergence control of Nut grass and Mullumbimby couch in certain species of established turf. Use is proposed in NSW and Queensland only.

The National Registration Authority for Agricultural and Veterinary Chemicals (NRA) invites public comment before deciding whether to proceed to approve this product for use in Australia.

The NRA has completed an assessment of the data submitted by the applicant in support of this use of halosulfuron-methyl and has provided the following information for public comment:

Agricultural Aspects

Halosulfuron-methyl is a new sulfonylurea compound for the selective control of the perennial sedge species, Nutgrass *(Cyperus rotundus)* and Mullumbimby couch *(Cyperus brevifolius),* in turf.

Halosulfuron-methyl will be applied to turf by boom spray equipment at 65 to 130 grams of product per hectare, depending on the density of the weed infestations. Spot treatment using a handgun or knapsack sprayer may be carried out using l.3grams of product per 100 square metres. A follow-up treatment may be required if there is sufficient new weed growth.

Efficacy trials carried out in eastern Australia indicated good control of Nut grass and Mullumbimby couch in warm season turf and there was no evidence of phytotoxicity in the turf species tested. Information from the United States indicates low phytotoxicity to cool season grasses. Advantages of halosulfuron-methyl include less phytotoxicity to grass species and better control than the limited chemical treatments currently available.

Environmental Aspects

Halosulfuron-methyl is moderately to highly soluble and hydrolytically unstable. Residues that are not taken up by plants are expected to become mainly associated with the interstitial water in the soil following application. Soil degradation occurs by hydrolysis at a rate which increases with increasing pH. Significant microbial degradation in soil is also likely.

Halosulfuron-methyl is likely to have low persistence in the soil or water. Accumulation of halosulfuron-methyl or its primary metabolites in the soil or in biota is not anticipated. Halosulfuron-methyl and its primary metabolites are unlikely to leach to groundwater.

The ecotoxicological profile of halosulfuron-methyl indicates low toxicity to birds, aquatic fauna, animals and bees. Hazard to non-target vegetation is variable, but is likely to be significant to some species if sprayed directly. The product label will warn users to avoid spraying non-target vegetation.

Like other sulfonylureas, halosulfuron-methyl is highly toxic to green algae and duckweed. However, significant aquatic exposure is not expected given the proposed use pattern and limited aquatic persistence.

Public Health Aspects

Like most other sulfonylurea herbicides, halosulfuron-methyl has low acute toxicity following oral, dermal or inhalational exposure. Its potential to cause eye irritation is rated as slight and it is not a skin irritant or skin sensitiser. A powder form of the SEMPRA 75% granular formulation had similar low toxicity, apart from demonstrating slight skin, in addition to eye, irritancy.

There were no consistent indications of any particular target organ toxicity in repeated dose studies in rats, mice or dogs. Dogs were most sensitive to the relatively nonspecific effects of chronic halosulfuron-methyl dosing (decreased weight gain and minor disturbances of blood biochemistry).

Halosulfuron-methyl was not carcinogenic or genotoxic and did not affect fertility in studies over two generations in rats. It does not have any significant potential to cause birth defects.

Based on an assessment of the toxicology and the fact that there should be no dietary intake of residues, it was considered that there should be no adverse effects on human health from the use of SEMPRA HERBICIDE for weed control in turf.

Residues in Food Commodities

SEMPRA HERBICIDE is for use on turf which will not produce food for human consumption.

The product label will include the instructions not to feed grass clippings from treated areas to poultry or other livestock and not to allow grazing of treated turf.

International Trade

The product is not intended for use on crops which will produce produce for export at this time.

Occupational Health and Safety

Halosulfuron-methyl is not a hazardous substance in accordance with the National Occupational Health and Safety Commission (NOHSC) Approved Criteria for Classifying Hazardous Substances [NOHSC: I008(1994)].

The formulated product SEMPRA HERBICIDE is considered hazardous by Worksafe Australia in accordance with the NOHSC Approved Criteria for Classifying Hazardous Substances [NOHSC:1008(1994)].

Hazardous substances are subject to the workplace controls outlined in the NOHSC Control of Hazardous Substances [NOHSC:1005(1994), 2007(1994)].

SEMPRA HERBICIDE is imported fully formulated and packed, ready to use on amenity turf areas. It has low toxicity by the oral, dermal and inhalational routes but is a slight skin and eye irritant. End users are instructed to avoid contact with eyes and skin and Worksafe Australia does not believe that any additional control in the form of personal protective equipment is necessary.

The Material Safety Data Sheet for SEMPRA HERBICIDE provides sufficient health and safety information. It should be available to all product handlers.

SEMPRA HERBICIDE containing halosulfuron-methyl can be used safely with the control measures described above.

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INTRODUCTION

The purpose of this document is to provide the public with a summary of the data reviewed and an outline of the regulatory considerations for the proposed application of the chemical halosulfuron-methyl as a herbicide for the control of Nut grass and Mullumbimby couch in turf areas such as turf production farms, golf courses, ovals, parks and gardens and to seek public comment prior to the 'chemical product being approved for use in Australia.

Comments should be received by 16 September 1994 and sent to:

Mr C Byrnes
Agricultural Registration
National Registration Authority
PO Box 240
Queen Victoria Terrace ACT 2600

TEL: (06) 272 4850
FAX: (06) 272 3218

Applicant

Monsanto Australia Limited has applied for clearance and registration of a herbicide product containing a new active constituent, halosulfuron-methyl, a new sulfonylurea compound which controls the sedges Nutgrass and Mullumbimby couch in established turf.

Product Details

Halosulfuron-methyl will be marketed under the trade name SEMPRA HERBICIDE as a dry flowable (water dispersible granule) formulation containing 750 g/kg of active constituent.

SEMPRA HERBICIDE will be imported fully formulated and packaged from the United States.

Monsanto Australia Limited intends to market SEMPRA HERBICIDE in NSW and Queensland initially for the control of the perennial sedges Nutgrass *(Cyperus rotundus)* and Mullumbimby couch (*Cyperus brevifoliusl)* in the turf species buffalo grass, carpet grass, durban grass, kikuyu grass, couch, hybrid couch and Queensland blue couch.

Overseas Registration Status

The US EPA has granted experimental use permits for a number of products containing halosulfuron-methyl. Full registration is pending for use in turf, corn, and sorghum in the USA and for use in sugarcane in Brazil.

PROPERTIES OF THE CHEMICAL ACTIVE INGREDIENT

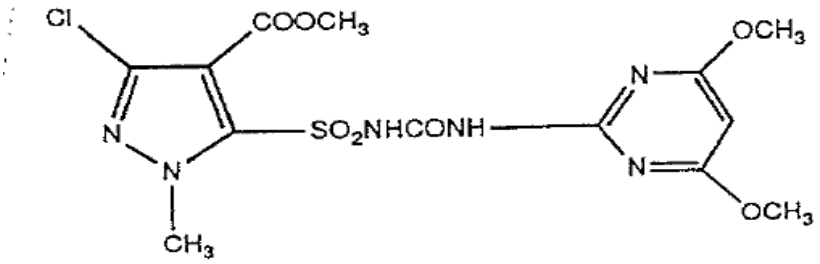
The chemical active ingredient halosulfuron-methyl is manufactured in Japan and has the following properties:

Common name:	halosulfuron-methyl (proposed)
Chemical name:	1H-pyrazole-4-carboxylic acid, 3-chloro-5-[[[[(4,6-dimethoxy-2-pyrimidinyl)amino]carbonyl]amino] sulfonyl]-1-methyl-,methyl ester
CAS registry number:	100784-20-1
Empirical formula:	$C_{13}H_{I5}N_60_7SCI$
Molecular weight:	434.82
Physical form:	powdered solid
Colour:	light white
Odour:	odourless
Melting Point:	175.5° to 177.2°C
Density:	1.618 g/mL at 25°C
Octanol/water partition coefficient:	

pH	Log K_{ow} at 23°C
5	1.67
7	-0.0186
9	-0.542

Vapour pressure: Less than 1 x 10^{-7} mm Hg at 25°C

Structural Formula:



AGRICULTURAL ASSESSMENT

Justification for Use

The perennial sedge species Nutgrass *(Cyperus rotundus)* and Mullumbimby couch *(Cyperus brevifolius)* are significant weeds of warm season turf on the eastern seaboard of Australia. These weeds detract from the appearance of turf areas, necessitating frequent close mowing during the summer months. Nutgrass can detract from the trueness of playing surfaces and turf managers therefore regard control of the weed as very important.

Currently available chemical control methods are limited in range and long term effectiveness. DSMA can be used on couch, bent and buffalo turf grass but it can be phytotoxic in hot, dry conditions. This chemical cannot be used for phytotoxicity reasons on turf containing Queensland blue couch, carpet grass, paspalum or kikuyu. This treatment does not provide long term weed control.

Treatments combining bentazone, MCPA and dicamba can be used on turf containing Queensland blue couch but effectiveness is limited and some phytotoxicity can occur. This treatment also depends on vigorous competition from the turf species and/or seasonal decline in the sedges at the end of the growing season.

The economic and technical advantages offered by the use of halosulfuron-methyl for control of Nut grass and Mullumbimby couch in turf include:

- absence of phytotoxicity to warm season turf species, and low phytotoxicity to cool season grass species
- superior season-long control can be achieved with one or two applications at recommended rates
- lower toxicity of the product to users and to the environment when compared to current treatments.

Proposed Use Pattern

The product can be used for control of Nut grass and Mullumbimby couch in established turf comprising the following species: Buffalo grass, Carpet grass, Durban grass, Kikuyu grass, Couch grass, Hybrid couch grass or Queensland blue couch in NSW and Queensland only. It should not be used on turf greens, as trials with the product in this situation have not been finalised.

Application rates of 65 to 130g of product per hectare are recommended. The higher rate is to be used where there are dense infestations of the weeds. Application should be made by boom sprayer with flat fan nozzles applying at least 80 L of water per hectare.

For smaller areas, application by handgun or knapsack sprayer may be made. The rate of application for this method is 1.3g of product per 100 square metres.

Using either method of application, the spray should be applied to actively growing weeds when new leaf growth has reached a minimum of 5cm on Nutgrass or 2cm on Mullumbimby couch. Turf should not be mowed for at least 2 days after treatment.

Follow-up treatments, up to a maximum of 260g/ha applied per season, may be required if there is sufficient new growth of weeds.

Evaluation of Efficacy

In Australia, formulations of halosulfuron-methyl have been evaluated in 21 experiments along the eastern seaboard from Cairns to Sydney during 1990 to 1992. Experiments were located in a range of situations including surrounds of golf greens and tees, fairways and fairway roughs. Three wettable powder formulations were evaluated containing 100g/kg, 253g/kg or 500g/kg of the active constituent. The formulations did not differ in their biological activity.

Efficacy assessment was made on a subjective basis using the Research System Scale (1-100) or objectively by counting emerged weed shoots in 0.1 or 0.25 square metre quadrats and calculating a percentage control as compared to populations in untreated controls.

In experiments on Nutgrass control, rates of application ranged from 50g active ingredient (ai) to 200g ai per hectare, and most trials included split applications of 2x50g and 2x100g ai/ha. A commercial standard, usually bentazone/dicamba/MCPA mixture, was used in most trials.

Symptoms of the halosulfuron-methyl treatments were gradual yellowing of sedges, taking up to approximately 6 weeks to full activity, including shoot death and disintegration of above ground

plant tissue. New germinations and/or regrowth from underground parts becomes apparent after 2 months. However, the average level of control from 50g ai/ha was still commercially acceptable 2-3 months after application but was reduced to less than 80% by 4-5 months after application.

The results indicate that good season-long control can be achieved by two applications of between 50 and 100g ai/ha (65 to 130g product/ha).

Six trials were conducted to assess efficacy against Mullumbimby couch. Results were very similar to those achieved with Nutgrass.

Trials were conducted on the effect of mowing, which showed that mowing should be delayed for 2 days after application, and on rainfastness, which showed that only a short rain-free period (2 hours) was needed.

Phytotoxicity

Safety to turf species was evaluated during the efficacy trials. A further trial was conducted specifically to examine phytotoxicity to *S* turf species at rates up to 200g ai/ha.

No significant adverse effects were reported except for one kikuyu trial where some phytotoxicity at rates above those to be included on the label occurred to grass under stress due to water-logging. This was considered an anomalous result.

Data from the US was also presented to indicate lack of phytotoxicity to cool season grasses, even at the seedling stage and at rates up to 275g ai/ha. Although registration is sought for warm season species, cool season grasses are often a desirable component of the turf. Use of the product is unlikely to result in damage to mixed warm and cool season grass turf.

ENVIRONMENTAL ASSESSMENT

Environmental Fate

Halosulfuron-methyl is a moderately to highly soluble and hydrolytically unstable sulfonylurea herbicide. Residues that are not taken up by plants are expected to become associated with interstitial water in the soil.

Abiotic processes (hydrolysis, photolysis)

Halosulfuron-methyl appears photostable in solution and on the surface of soil. However, it is hydrolytically unstable at all pH levels likely to be encountered in the environment. Half-lives are about 27 days, 14 days and 19 hours, respectively, at pH 5, 7 and 9. At pH 5, hydrolysis proceeds via cleavage of the sulfonylurea link to produce amine and sulphonamide fragments. At pH 9, hydrolysis of the sulfonylurea link is more rapid and accompanied by rearrangement, in which the pyrimidine and pyrazole rings become linked by an amino group. At neutral pH, both mechanisms operate, the latter being approximately twice as fast. Some hydrolysis (in the order of 5%) of the carboxylic ester is also evident at neutral pH.

Metabolism in soils

Similar pH dependent degradation is observed in soils. Results from studies on an acidic silty clay loam and an alkaline sandy loam indicate that both hydrolytic and microbial mechanisms operate, the latter evident from the production of carbon dioxide from either ring, particularly at alkaline pH. Other routes observed for soil metabolism include elimination of dimethyl malonate to form a guanidine derivative.

Half-lives for the parent compound are in the order of 1-2 weeks. Amine and sulphonamide metabolites from cleavage of the sulfonylurea link are slightly more persistent than the parent, but degrade further to bound residues and carbon dioxide in aerobic soils. These primary metabolites persist under anaerobic conditions.

Mobility in soils

Soil organic carbon partition coefficients obtained from standard adsorption/desorption tests on four soils ranged between 28 and 178, indicating that halosulfuron-methyl is typical of the sulfonylureas in sorbing rather weakly to soil, and having moderate to high mobility. The herbicide would have been almost completely ionised in solution as the pH of all soils was at least two units above the pKa.

Field dissipation

Field studies at four sites in the US indicated that only small proportions (max 1.2% of applied) of halosulfuron-methyl degradates leached through 90cmc lysimeters. Half-lives in field soils ranged between 6 and 34 days, increasing to 56 days over the North American winter.

Accumulation in soils and biota

Accumulation of halosulfuron-methyl in soils is not expected as it will be applied at most twice per season and has limited persistence. Metabolites are also not expected to accumulate as they too do not persist in soils. Similarly, bioaccumulation would not be expected given the hydrophilicity and hydrolytic instability of halosulfuron-methyl.

Environmental Effects

The ecotoxicological profile is typical for a sulfonylurea, with herbicidal activity the dominant feature.

Avian toxicity

Halosulfuron-methyl proved practically non-toxic to bobwhite quail and mallard ducks exposed via acute oral or dietary routes.

Aquatic toxicity

Halosulfuron-methyl is practically nontoxic to aquatic fauna. No effects could be discerned in warm and cold water fish and cladocerans exposed to saturated, neutral, unbuffered solutions of halo sulfur on-methyl (measured concentrations in the order of 25 mg/L).

Halosulfuron-methyl was very highly toxic to freshwater algae and duckweed in laboratory growth inhibition tests, with decreased frond production in the latter at concentrations in the order of 0.04ppb.

Non-target invertebrates

Halosulfuron-methyl proved practically nontoxic to bees exposed via the contact route.

Non-target plants

Halosulfuron-methyl is said to be selective for sedges and certain annual broad leafed weeds in warm season turf species.

Environmental Hazard

Terrestrial organisms will not undergo significant exposure to halosulfuron-methyl as it will be applied no more than twice a year at a relatively low rate. Hazard to terrestrial fauna is minimal as the herbicide does not exhibit significant toxicity.

If halosulfuron-methyl were to be sprayed inadvertently over 15cm of standing water at the maximum proposed rate, a concentration of about 70ppb would prevail, more than two orders of magnitude below no effect levels for aquatic fauna. Hazard to aquatic fauna is minimal.

For a more realistic exposure scenario via runoff, concentrations in the order of 5% of those from direct overspray may result, or about 3.5ppb. Such concentrations would inhibit the growth of green algae and duckweed. However, halosulfuron-methyl has limited aquatic persistence, and brief exposures of this magnitude should not result in permanent damage to aquatic flora. In addition, runoff from proposed use sites is likely to be mainly to artificial situations such as stormwater drains and retention ponds, rather than natural areas. The label contains warnings to minimise the risk of aquatic contamination.

Hazard to non-target vegetation would be variable, but likely to be significant for some species if sprayed directly. The label warns against direct application to desirable plants.

Data submitted support the conclusion that use of SEMPRA on turf according to label and good agricultural practice should not lead to significant environmental contamination or damage to non-target fauna and flora. In order to help validate this assessment, the company has agreed to alert the Environment Protection Agency immediately of any off-target incidents associated with the use of SEMPRA that may arise.

PUBLIC HEALTH AND SAFETY ASSESSMENT

Evaluation of Toxicology

The toxicological database for halosulfuron-methyl, 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 which are high compared to likely human exposures. The use of high doses increases the likelihood that potentially significant toxic effects will be identified. 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 at which no adverse health effects in humans would be expected.

Toxicokinetics and Metabolism

Rats given oral doses of halosulfuron-methyl cleared equal amounts via the urine within 12 hours and via the faeces within 2 days. Residues in the rat carcasses were less than 1% of the dose after 7 days. Major urinary metabolites were the demethylated and hydroxylated products. In lactating goats given radio-labelled halosulfuron by capsule for 4 days, less than 0.1% was excreted in milk.

Acute Studies

Like other sulfonylurea herbicides, halosulfuron-methyl has low acute toxicity. In rats and mice oral lethal doses were in excess of 8000 mg/kg body wt. Toxicity by the dermal and inhalational routes was also low. It was a slight eye irritant (rabbits) but was not a skin irritant (rabbits) or skin sensitiser (guinea pigs).

A powder form of the SEMPRA granule formulation had similar low oral, dermal and inhalational toxicity in rats. This formulation was a slight skin and eye irritant in rabbits. These data confirm the very low risk of acute poisoning with the formulated product, but indicate the need to prevent exposure to the skin and eyes.

Repeat-Dose Studies

Halosulfuron-methyl had low toxicity in repeat-dose dietary studies in rodents. Toxic effects in all species were relatively non-specific and no primary target organ for toxicity was identified. In long-term studies, NOELs were about 410 mg/kg body wt/day (male mice), 1215 mg/kg body wt/day (female mice), 108 mg/kg body wt/day (male rats) and 56 mg/kg body wt/day (female rats), on the basis of an equivocal increase in deposits in the testes in male mice at higher doses and a depression of bodyweight gain in rats at higher doses. The lowest NOEL of 1mg/kg body wt/day was established in male dogs in a 1-year oral dosing study, based on reduced body weight gains and blood cholesterol levels at the next highest dose of 10 mg/kg body wt/day.

Carcinogenicity Studies

Halosulfuron-methyl was administered in the diet for 18 months to mice (up to 1000 mg/kg body wt/day) and in rats for 24 months (up to 140-220 mg/kg body wt/day). There was no evidence of tumour induction in either species.

Reproduction and Developmental Studies

Halosulfuron-methyl was administered in the diet to Sprague-Dawley rats for two generations. There were no effects on reproductive capacity or on fertility. Reduced parental body weight gain and reduced pup weights occurred at the highest dose of 274 mg/kg/day.

In pregnant rats given halosulfuron-methyl by gavage at 0, 75, 250 and 750 mg/kg/day during the critical periods of foetal development, the incidences of foetal abnormalities and variations were slightly increased at the highest dose, which also caused significant maternal toxicity (clinical signs and reduced weight gain) and fetotoxicity (decreased foetal weights and increased uterine death). In another study in rats at doses up to 300 mg/kg body wt/day, there was no evidence of toxicity to

the mothers or foetuses. Similarly, halosulfuron-methyl did not cause foetal abnormalities in rabbits at oral doses up to 150 mg/kg body wt/day.

Genotoxicity Studies

Halosulfuron-methyl was not mutagenic in bacterial and mammalian cells in vitro, did not cause chromosomal aberrations in vivo or in vitro, and did not cause unscheduled DNA synthesis in rat hepatocytes. These studies indicate that halosulfuron-methyl is not genotoxic.

Public Health Standards

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.

The NDPSC recommended that halosulfuron-methyl be listed in Schedule 5 of the Standard for the Uniform Scheduling of Drugs and Poisons (SUSDP). There are provisions for appropriate warning statements and first-aid directions on the product label.

Potential for Residues in Food for Humans

The product is for use on turf grasses only at this time. The only potential for residues in food for humans would arise through the consumption of animals which have been fed grass clippings from treated areas or which have grazed treated areas.

The product label will include instructions not to feed grass clippings from treated areas to poultry of other livestock or to allow grazing of treated turf. This is standard practice for products for use on turf.

International Trade

The product is to be used on turf only at this time. There is therefore no produce to be sold on the international market which may contain residues of halosulfuron-methyl.

OCCUPATIONAL HEALTH AND SAFETY

Active constituent

Halosulfuron-methyl is not a hazardous substance. It was screened through the Health Effects Criteria, in the order given in the National Occupational Health and Safety Commission (NOHSC) Approved Criteria for Classifying Hazardous Substances.

Halosulfuron-methyl will at present be imported as formulated product, so no Australian workers will handle the active constituent alone.

According to Monsanto Australia Limited, halosulfuron-methyl is not classified as a dangerous good under the Australian Code for the Transport of Dangerous Goods by Road and Rail (ADG Code). Therefore transport workers do not need to adhere to any special conditions when transporting it.

Halosulfuron-methyl has low acute toxicity by the oral, dermal and inhalational routes and is a slight eye irritant. The detailed discussion of toxicity occurs elsewhere in this Public Release Summary.

End Use Product

SEMPRA HERBICIDE is a hazardous substance. It was screened through the Health Effects Criteria, in the order given in the National Occupational Health and Safety Commission (NOHSC) Approved Criteria for Classifying Hazardous Substances. It was determined to be hazardous on the basis of acute oral toxicity.

It is imported fully packed as dry flowable water-dispersible granules, in plastic containers inside cardboard boxes containing 100g or 600g of product.

Hazardous substances are subject to the workplace controls outlined in the NOHSC Control of Hazardous Substances.

Manufacture and formulation

Australian workers are not involved in the manufacture or formulation of halosulfuron-methyl or its product at this time.

Transport, storage and retail

As SEMPRA HERBICIDE will be imported finally packed into Australia, only transport, storage and retailing workers will handle it before end use. These workers could only become contaminated with the product under accidental conditions, for instance if the packaging were breached.

The product is not classified as a dangerous good under the ADG Code.

The risk of exposure to these workers is small and would involve low health and safety risks. The Safe Handling Information section in the Material Safety Data Sheet (MSDS) and the instructions on the label for the product provide sufficient information to enable workers to deal with spills.

End-use including subsequent exposure to treated areas

SEMPRA HERBICIDE will be applied by boom spray to control Nutgrass and Mullumbimby couch in warm season turf. Monsanto Australia Limited suggests that the largest group of users will be amenity grass managers. Application rates per hectare for the product range between 65 and 130g per hectare, with ,a maximum annual application of 260g/ha. The concentration of halosulfuron-methyl in the applied spray ranges from 0.06% to 0.12%.

End users are most likely to be contaminated with the product via the skin. Acute toxicity of the product is such that end users are advised on the product label to avoid contact with eyes and skin. Worksafe Australia does not believe that any additional control by utilising personal protective equipment (PPE) is necessary, so PPE is not included on the label safety directions.

Based on the results of a long-term feeding experiment in dogs, Worksafe Australia does not believe that workers managing large or small areas of turf are at risk of suffering health effects from the long-term use of this product.

A restriction on entry into treated areas is not indicated at this stage, based on the low dermal and inhalational toxicity of SEMPRA HERBICIDE. Monsanto Australia Limited have elected to add the following a conservative re-entry restriction on the label to avoid unnecessary exposure to people and pets - "Keep people and pets off treated areas until the spray solution has dried".

Material Safety Data Sheet

The manufacturers of SEMPRA HERBICIDE have produced a MSDS for the product. Employers should obtain these from the supplier and ensure that all their employees have ready access to it.

Workers using SEMPRA HERBICIDE or any hazardous halosulfuron-methyl products in the future should read the MSDS.

Transport workers, storage personnel and retail workers should use the Safe Handling Information in the MSDS and the label instructions for dealing with accidental exposure to the product.

LABELLING

The proposed label for SEMPRA HERBICIDE is attached as Appendix I.

SUGGESTED FURTHER READING

A document giving the more detailed technical assessments of occupational health and safety, public health and environmental impact is available on request from the NRA. Please contact David Hutchison, telephone 06 271 6384, fax 06 272 3218, if you wish to receive a copy.

The following publications also provide further general information on requirements and standards:

Interim Requirements for the Registration of Agricultural and Veterinary Chemical Products (available from the NRA)

Code of Practice for Labelling Agricultural Chemical Products (available from the NRA)

Code of Practice for Labelling Veterinary Chemical Products (available from the NRA)

MRL Standard - Maximum residue limits in food and animal feedstuffs (NHMRC)

Approved Criteria for Classifying Hazardous Substances National Occupational Health and Safety Commission, [NOHSC:1008(1994)], Australian Government Publishing Service, Canberra, 1994.

Australian Code for the Transport of Dangerous Goods by Road and Rail, 5th Edition

Federal Office of Road Safety, Australian Government Publishing Service, Canberra, September, 1992.

Control of Workplace Hazardous Substances National Occupational Health and Safety Commission, [NOHSC:1005(1994),2007(1994)], Australian Government Publishing Service, Canberra, 1994.

Container Label: Front Panel

DRAFT LABEL (8 August 1994)

WARNING

KEEP OUT OF REACH OF CHILDREN
READ SAFETY DIRECTIONS BEFORE OPENING

Sempra®

herbicide by Monsanto

ACTIVE CONSTITUENT: 750 g/kg HALOSULFURON-METHYL

For selective post-emergence control of Nutgrass and Mullumbimby couch in turf, as per directions for use.

READ THE ENCLOSED BOOKLET BEFORE USING THIS PRODUCT

Monsanto Australia Limited (A.C.N. 006 725 560)
600 St Kilda Road, Melbourne 3004
NET CONTENTS 100g or 600g

Sempra\100\600\0894\1.2

N.R.A.
APPROVED DRAFT
Date 15/8/94

Container Label: Back Panel

DRAFT LABEL (8 August 1994)

Sempra® herbicide by Monsanto

Safety Directions

Harmful if swallowed.

Dust will irritate the eyes.

Avoid contact with eyes and skin.

Wash hands after use.

First Aid

If poisoning occurs, contact a doctor or Poisons Information Centre.

SPECIALIST ADVICE IN EMERGENCY: PHONE 008 033 111

All Hours, Australia-wide

Refer to Monsanto Material Safety Data Sheet No. 238

Monsanto (logo)

Monsanto Australia Limited ACN 006 725 560

600 St Kilda Road Melbourne 3004

Sempra\100\600\0894\2.2

Box Label: Front Panel

DRAFT LABEL (8 August 1994)

WARNING

KEEP OUT OF REACH OF CHILDREN

READ SAFETY DIRECTIONS BEFORE OPENING

Sempra®

herbicide by Monsanto

ACTIVE CONSTITUENT: 750 g/kg HALOSULFURON-METHYL

For selective post-emergence control of Nutgrass and Mullumbimby couch in turf, as per directions for use.

READ THE ENCLOSED BOOKLET BEFORE USING THIS PRODUCT

Monsanto Australia Limited (A.C.N. 006 725 560)

600 St Kilda Road, Melbourne 3004

NET CONTENTS 100g or 600g

Sempra\100\600\0894\BOX1.2

Box Label: Back Panel

DRAFT LABEL (8 August 1994)

Sempra® herbicide by Monsanto

Safety Directions

Harmful if swallowed.

Dust will irritate the eyes.

Avoid contact with eyes and skin.

Wash hands after use.

First Aid

If poisoning occurs, contact a doctor or Poisons Information Centre.

Limit of Warranty and Liability

Monsanto Australia Limited (" Monsanto") warrants that this product conforms to the chemical description on the label. As the use of product sold is beyond the control of Monsanto, no responsibility whatsoever for any consequences is accepted in respect of this product, save those non-excludable conditions implied by any State and Federal legislation or law of a Territory.

Not for re-packaging or re-formulation. No licence under any non-Australian patent is granted or implied by purchase of this product.

SPECIALIST ADVICE IN EMERGENCY: PHONE 008 033 111
All Hours, Australia-wide
Refer to Monsanto Material Safety Data Sheet No. 238

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Monsanto Australia Limited ACN 006 725 560
600 St Kilda Road Melbourne 3004

BAR CODE 9313771XXXX

Sempra\100\600\0894\BOX2.2

Booklet

DRAFT LABEL (8 August 1994)

Sempra®

herbicide by Monsanto

DIRECTIONS FOR USE

For selective post-emergence control of Nutgrass and Mullumbimby couch in turf, as per directions for use.

For complete directions for use, read this booklet.

Sempra\100\600\0894\BK

DIRECTIONS FOR USE (NSW AND OLD ONLY)

RESTRAINTS

DO NOT use on turf greens

DO NOT apply more than 260 g/ha per season

DO NOT apply after the onset of frosts

Situation	Weeds Controlled	Rate	Critical Comments
Established turf as named:- Buffalo grass *(Stenotaphrum secundatum)* Carpet grass *(Axonopus affinis)* Durban grass *Dactyloctenium australe)*	Nutgrass *(Cyperus rotundus)* Mullumbimby couch *(Cyperus brevifolius)*	65-130 grams per hectare	Use higher rates on dense infestations. Apply to actively growing weeds when new leaf growth has reached a minimum of 5 cm on Nutgrass or 2 cm on Mullumbimby couch. Apply using a boom spray with flat fan nozzles to apply at least 80 L/ha of water. Apply follow-up treatments if sufficient new growth warrants re-treatment. For optimum control, mowing should be delayed for 2 days following treatment.
Kikuyu grass *(Pennisetum clandestinurm)* Couch *(Cynodon dactylon)* Couch, hybrid *(Cynodon dactylon x* C.		1.3	Use of this product on newly seeded, sodded, or sprigged turfgrass that is not well established may result in damage and/or delayed establishment. In addition, application to turf weakened by weather conditions or by physical damage due to intensive use or cultural practices such as scarification, coring, aeration or top-dressing, may result in damage and/or delayed recovery.

DO NOT apply this product through any type of irrigation system

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

GENERAL INSTRUCTIONS

Sempra herbicide can be used for selective control of Nutgrass *(Cyperus rotundus)* and Mullumbimby couch *(Cyperus brevifolius)* in turf as named in the **Directions for Use** table.

Symptoms of weed control are a gradual yellowing of foliage and seed heads followed by desiccation. Initial symptoms may take 7-10 days to be noticeable, with full effects occurring 4 to 6 weeks after treatment.

Sempra should be applied to actively growing weeds when new growth has reached a minimum of 5 cm of new leaf growth for Nutgrass or 2 cm for Mullumbimby couch. Apply follow-up treatments if sufficient new growth warrants re-treatment.

Irrigation or rainfall within two hours of application will reduce control. Drought stress after treatment may also reduce control.

Mixing

Sempra is a dry flowable granule which disperses in water. Add the measured amount gradually to a part-filled spray tank while maintaining continuous bypass agitation. Add the surfactant near the end of the filling process to avoid excessive foaming. Remove the hose from the mixing tank immediately after filling to avoid siphoning back into the water source. If allowed to stand, ensure that the mixture is thoroughly agitated before recommencing spraying. Use the mixture within one day.

Sprayer cleanup

Before application of products other than Sempra, the sprayer must be cleaned out as follows:

1. Drain the tank and flush equipment with water for a minimum of 10 minutes, including hoses, filters and boom.
2. Fill the tank with clean water and add chlorine bleach (containing 4% chlorine) at the rate of 300ml/100L of water. Flush through the boom and then agitate for 15 minutes.
3. Repeat step 2 above.
4. Remove all nozzles and screens and clean thoroughly.
5. To remove traces of chlorine bleach, rinse the tank thoroughly with clean water and flush through hoses and boom.

Caution: Do not use chlorine bleach with ammonia. All traces of liquid fertilizer containing ammonia, ammonium nitrate or ammonium sulphate must be rinsed with water from the mixing and application equipment before adding chlorine bleach solution. Failure to do so will release a gas with a musty chlorine odour which can cause eye, nose, throat and lung irritation. Do not clean equipment in an enclosed area.

Storage and Disposal

Store in the closed, original container in a well-ventilated area, as cool as possible. Avoid prolonged storage in direct sunlight. Do not contaminate seed, food, feedstuffs or water by storage or disposal.

Triple rinse the empty container and add the rinsate to the spray tank or discard with the empty container. Dispose of the container and/or rinsate by burial under at least 500 mm of soil at an approved disposal site in a non-crop, non-pasture area away from water sources or homes. Empty containers should not be burnt and should be punctured, crushed or broken before disposal.

Safety Directions

Harmful if swallowed.

Dust will irritate the eyes.

Avoid contact with eyes and skin.

Wash hands after use.

First Aid

If poisoning occurs, contact a doctor or Poisons Information Centre.

Limit of Warranty and Liability

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SPECIALIST ADVICE IN EMERGENCY: PHONE 008 033 111

All Hours, Australia-wide

Refer to Monsanto Material Safety Data Sheet No. 238

Monsanto Australia Limited ACN 006 725 560
600 St Kilda Road Melbourne 3004

Surfactant Addition

Sempra must be applied with a non-ionic surfactant to ensure uptake. Use 200mL/100L of a 600 g/L non-ionic surfactant or equivalent. For hand-gun or knapsack application, add surfactant at 20mL/10L of water.

Compatibility

Sempra is compatible with Hoegrass[1], dicamba/MCPA and bromoxynil/MCPA mixtures.

Protection of Crop, Native and Other Non-target Plants

Avoid spraying of non-target vegetation.

Do not use clippings from treated areas for mulching around vegetables or fruit trees.

Protection of Livestock, Wildlife, Fish, Crustacea, the Environment and Others

Do not contaminate dams, rivers, or streams with the product or used container.

Do not feed grass clippings from treated areas to poultry or other .livestock or allow grazing of treated turf.

Keep people and pets off treated areas until the spray solution has dried.

National Registration Authority
For Agricultural & Veterinary Chemicals

First Floor, Industry House, National Circuit, Barton ACT
PO Box 240. Queen Victoria Terrace. Parkes ACT 2600 Australia
Tel: (06) 272 5158 Fax: (06) 272 4753

Technical Assessment Reports

Halosulfuron·methyl

In The Product

SEMPRA HERBICIDE BY MONSANTO

This document contains the detailed technical assessment reports provided to the NRA by the advisory agencies. The reports have not been edited by the NRA (except to remove confidential formulation information) and are provided to supplement the information contained in the Public Release Summary.

Note that some of these reports refer to MONTURF HERBICIDE. This is the earlier name for the product proposed by Monsanto Australia Limited. Following registration of the trade mark SEMPRA, the product will now be known as SEMPRA HERBICIDE.

Public Health and Safety Assessment

Halosulfuron-methyl

In the Product

SEMPRA HERBICIDE BY MONSANTO

Prepared by
Chemical Safety Unit
Department of Human Services and Health

HALOSULFURON-METHYL

Product: MONTURF Herbicide
Company: Monsanto Australia Limited

SUMMARY (November 1993)

Introduction

Halosulfuron-methyl (henceforth referred to as halosulfuron) is a new sulfonyl urea herbicide which is claimed to have unique post-emergent activity on Cyperus spp and excellent safety on turf species. It is a proprietary chemical of Nissan Chemical Industries Ltd, Japan, to be marketed in Australia by Monsanto Australia Limited. This application is for TGAC clearance of the active, for poison scheduling and for approval of a 750 g/kg EUP, 'MONTURF' Herbicide for use on certain weeds in turf ie. This application is for non-crop use.

Toxicokinetics and Metabolism

Sprague-Dawley rats were given PO doses of halosulfuron. Near equal proportions were eliminated in faeces and urine. Most urinary radioactivity was eliminated within 12h, that in faeces within 2d. Females excreted somewhat less in urine than males but only slightly more in faeces; at 7 days, carcass residues were less than 1% of the dose; in females they were slightly higher than in males. The extent of PO absorption of halosulfuron in rats is not known but would not be less than about 50%. Major urinary metabolites were desmethyl-halosulfuron (50-70% of urinary activity) and 5-hydroxydesmethyl-halosulfuron (tentatively identified; 20-40%). Minor metabolites included 4, 6-dihydroxy-halosulfuron, N-demethyl-halosulfuron, halosulfuron acid (only at a 250 mg/kg dose, not at 5 mg/kg) and 5-hydroxy-halosulfuron. Cleavage of the molecule to give separate ring metabolites represented only a minor pathway.

In lactating goats given 20 mg/day 14C-halosulfuron by capsule (approx. equivalent to 11 ppm in the diet) for 4 days, then sacrificed at 22h after the last dose, urine had about 85% of the total dose, faeces approx. 12% and milk, less than 0.1%. The majority of radioactivity was eliminated within 24h of each daily dose. The majority of radioactivity in urine was unchanged halosulfuron. The major residue in tissues was halosulfuron. Desmethyl-halosulfuron and halosulfuron acid were detected, primarily in liver and kidney.

Laying hens were given 14C-halosulfuron in capsules at 1.1 mg/day (equiv. to 10 ppm in the diet) for 4 days and sacrificed 22h after the last dose. The majority of radioactivity (95%) was in excreta, mostly excreted within 24h of each dose. Eggs and other tissues contained 0.2 and 0.5% of the total dose. Major radioactive components of excreta were halosulfuron and 5-hydroxy-halosulfuron.

Acute Studies

Halosulfuron had very low acute oral toxicity in rats and mice By the IP and SC routes it also had low to very low toxicity in rodents. It was of low to very low dermal and inhalational toxicity (rats), was not a skin irritant (rabbits) nor was it a skin sensitiser (guinea pigs). It was possibly a slight eye irritant.

MON 12022, the powder equivalent of MONTURF Herbicide, the 75%granule formulation to be used in Australia, was of low oral toxicity (rats) and low to very low dermal and inhalational toxicity (rats). It was a slight skin and eye irritant (rabbits). It was not a skin sensitiser (guinea pigs).

MON 12051, the powder equivalent of a 50.5% granule formulation, was of low oral toxicity (rats) and low to very low dermal and inhalational toxicity (rats). It was a slight skin and moderate eye irritant (rabbits). It was not a skin sensitiser (guinea pigs).

Short-Term Repeat-Dose Studies

Halosulfuron was administered to mice (10/sex/gp) at dietary levels of 0, 300, 1000, 3000 and 10000 ppm for 28 days. Bodywt gain was severely depressed at the HD, less so at 3000 ppm. At gross necropsy, centrilobular hypertrophy, vacuolation and slightly increased coagulative necrosis were noted in the liver of some HD animals. 2/10 HD males had alveolar/bronchiolar adenomas (typical of those found in CD-1 mice) and 1/10 HD females had an ovarian choriocarcinoma.

Halosulfuron was administered to Sprague Dawley rats (10/sex/gp) at dietary levels of a, 300, 1000, 3000 and 10000 ppm for 28 days. No compound-related effects were noted at 1000 ppm (approx. 100 mg/kg/d), with reduced bodywt gain and some pancreatic cell pathology at the next highest dose.

Halosulfuron was dermally applied to Sprague-Dawley rats (5/sex/group) at 0, 10, 100, 500 or 1000 mg/kg/day for 5 days; application was to shaved trunk skin (approx. 10% of body surface) on occluded, saline-dampened gauze pads. Dermal administration of up to 1000 mg/kg/day to Sprague-Dawley rats did not result in any clinical observations and/or gross necropsy findings suggestive of an effect of the test material.

Halosulfuron was applied to the skin of Sprague-Dawley rats (5/sex/group) at 0, 10, 100 or 1000 mg/kg/day for 21 consecutive days; application was to shaved trunk skin (approx. 10% of body surface) on occluded, saline-dampened gauze pads. There was little evidence of toxicity at the highest dose used.

In the first phase of a beagle dog study (1/sex), five rising doses from 50 up to 800 mg/kg (in gelatine capsules) were given for 4 days each (or 1 day for the last dose). Doses up to

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400 mg/kg/day did not cause any treatment-related effects. Within 3h after 800 mg/kg, both animals became sluggish and subdued, were unable to walk and had body tremors; both were sacrificed after 5h. In a second phase, dogs (1/sex) received 400 mg/kg PO halosulfuron for 2 days. The male was killed 6h after the second dose in a moribund condition so, following 10 days recovery, the female received 200 mg/kg/day for 14 days. The female vomited following the first dose but no clinical signs or effects on body weight or food consumption were observed thereafter. Slightly higher BUN and lower cholesterol levels were noted. There were no gross pathological findings.

Subchronic Studies

In a range-finding study, halosulfuron was administered in the diet to CD-1 mice (20/sex/group) at doses of 0, 350, 2100, 3500 or 7000 ppm for at least 13 weeks. At the HD there were reduced bodywt gains (males), and a low incidence of thymic lymphocytolysis and reticuloendothelial hyperplasia in various lymph nodes (females). The NOEL was 3500 ppm (approx. 500 mg/kg/d).

CD-1 mice (10/sex/group) were dosed with halosulfuron in the diet at levels of 0, 100, 400, 1600 and 6400 ppm for 13 weeks. A further 10/sex were included in the control and HD groups in order to determine the reversibility of any effects and kept for a 6-week recovery period. There were no signs of toxicity. The NOEL was in excess of 6400 ppm (males: 937-1506 mg/kg/day; females: 1203-2032 mg/kg/day).

Sprague-Dawley rats (20/sex/group) were fed halosulfuron in the diet at 0, 100, 400, 1600 or 6400 ppm for 13 weeks. The NOEL was 400 ppm (males 28.8 mg/kg/day, females 37.3 mg/kg/day), based on an increased incidence of haemosiderin deposition in the tubular epithelium of the kidneys at 1600 ppm and above. At the HD, reduced bodywt gain and several blood chemistry changes (reduced cholesterol and bilirubin, increased ALT) were noted.

Halosulfuron (98.5%) was administered in capsules to pure-bred beagles (4/sex/group) at dose levels of 0, 2.5, 10, 40 and 160 mg/kg/day for 13 weeks. The NOEL was considered to be 10 mg/kg/day, based on reduced bodywt gains at the next highest dose. At the HD, reduced Hb, PCV and RBC count were noted (females), as were WBC counts (males).

Chronic Studies

Halosulfuron (98.7%) was administered in the diet to Charles River CD-1 mice (75/sex/gp) at target concentrations of 0, 30, 300, 3000 and 7000 ppm for 18 months. In conclusion, the only evidence of toxicity was an equivocal increase in incidence of epididymal microconcretions in high dose males. The NOEL for chronic effects was at least 3000 ppm (410 mg/kg) in males and 7000 ppm (1214.6 mg/kg) in females.

Halosulfuron was administered in the diet to Sprague-Dawley (Crl:CDBR) rats (85/sex/gp) at target concentrations of 0, 10, 100, 1000 and 2500 ppm for 24 months; a sixth group of 85 males

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received 5000 ppm. The only evidence of toxicity was a body weight gain depression in high dose males and females. Halosulfuron did not produce an oncogenic response. The NOEL was 2500 ppm (108.3 mg/kg/dl in males and 1000 ppm (56.3 mg/kg/dl in females.

Halosulfuron was administered orally in gelatine capsules to beagle dogs (6/sex/gpl at doses of 0, 0.25, 1.0, 10 and 40 mg/kg/day for 12 months. Body weight gains, cholesterol levels and lymphocyte values were decreased in males and red cell parameters were decreased in females at 40 mg/kg. At 10 mg/kg, body weight gains and cholesterol levels were decreased in males. The NOEL was considered to be 1 mg/kg/day for males and 10 mg/kg/day for females.

Reproduction Studies

In a range-finding study, Sprague Dawley rats (10/sex/gpl) were fed diets containing halosulfuron at levels of 0, 100, 400, 1600 and 6400 ppm. Treatment was for 4 weeks prior to mating, throughout mating, gestation and lactation. Maternal and paternal toxicity was indicated at 6400 ppm by reduced weight gain during the treatment period. Wt gain was marginally reduced in females at 1600 ppm during gestation. The mean number of implantations was slightly reduced at 6400 ppm. Decreased litter and pup weights were observed at 1600 and 6400 ppm. The NOEL for parental F0 animals was 1600 ppm (about 150 mg/kg/d for males, 185 mg/kg/d for females) and for F1 offspring, 400 ppm (38 mg/kg/d for F0 males, 47 mg/kg/d for F0 females).

Halosulfuron was administered to Sprague-Dawley rats at dietary levels of 0, 100, 800 and 3600 ppm for two generations (dosing commencing 14 weeks prior to F0 matings). Reduced parental body weight gain and reduced pup weights occurred at 3600 ppm. There were no treatment related effects on reproductive or fertility parameters. The NOEL was 800 ppm (61 mg/kg/d for F0 males, 69.7 mg/kg/d for F0 females).

Developmental Studies

In a dose-selection study, halosulfuron was administered by gavage at a, 15, 50, 150 and 300 mg/kg/day to pregnant CD (SD) BR rats (6/gp) during gestation days 6 to 15, with necropsy on day 20. There were no significant treatment-related observations at the highest dose tested.

Halosulfuron was administered by gavage at a, 75, 250 and 750 mg/kg/day to pregnant CD (SD) BR rats (25/gp) during gestation days 6 through 15, with necropsy on day 20. Maternal toxicity was evident at 750 mg/kg by clinical signs and reduced wt gain. Fetotoxicity, as evidenced by decreased fetal wts and increased resorptions, was seen at the 750 mg/kg. The incidence of malformed fetuses (external, visceral and skeletal) was increased at this dose, as were several visceral and skeletal variations. Based on these results, the NOEL for both maternal and development toxicity was 250 mg/kg/day.

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In a range-finding rabbit teratology study, halosulfuron was administered by gavage at 0, 75, 250, 750 and 1000 mg/kg/day to artificially inseminated Hazleton HRA:(NZW)SPF rabbits (6/gp) during gestation days 7 to 19. Maternal toxicity was evidenced by reduced bodywt gains (slight at 75 mg/kg, severe at higher doses), abortions at 250 mg/kg and above, and mortalities at 750 mg/kg and above. Nonviable fetuses were seen at 250 mg/kg and above. Fetal bodywts were slightly reduced at 75 and 250 mg/kg (total litter losses at higher doses). Based on these results, the maternal and foetal NOELs would be less than the lowest dose tested of 75 mg/kg/day.

Halosulfuron was administered by gavage at doses of 0, 15, 50 and 150 mg/kg/day to mated female Hazleton HRA:(NZW)SPF rabbits (17/gp) during gestation days 7 to 19. Mean bodywt gain values indicated maternal toxicity at 150 mg/kg, with some evidence of embryotoxicity at the same dose. There was no evidence of teratogenicity. Under the study conditions, the NOEL was 50 mg/kg/d.

Genotoxicity Studies

In two 'in vitro' tests for gene mutations ('Salmonella typhimurium' Histidine Reversion Test and Chinese Hamster Ovary Cells in Culture: HGPRT Locus Mutation Test), there was no evidence that halosulfuron induced gene mutations. In two tests for induction of chromosomal aberrations (Mouse Micronucleus Test 'in vivo' and a Cytogenetics Assay in Chinese Hamster Ovary Cells in Culture), there was no evidence of a genotoxic effect of halosulfuron. Results in an Unscheduled DNA Synthesis Assay in rat primary hepatocytes were negative.

DISCUSSION

There is an extensive database in support of halosulfuron. Like other sulfonylurea herbicides previously evaluated (see Appendix I), halosulfuron has low acute and chronic toxicity. In rodents, its oral toxicity was very low while by the dermal and inhalational routes its acute toxicity was also low. It was not a skin irritant (rabbits) and was not a skin sensitiser (guinea pigs). Slight eye irritancy results (rabbits) were equivocal.

Halosulfuron had low toxicity in repeat-dose dietary studies in rodents. In short-term studies in mice and rats, no compound-related effects were noted at about 150 and 100 mg/kg/d, respectively, with some effects on the liver (both species) and on the pancreas (rats) at higher doses. In subchronic studies, higher no-effect levels in mice were reported at 500 to >1,000 mg/kg/d while in rats the NOEL was about 29 (males) to 37 mg/kg (females), based on minimal biochemistry changes and haemosiderin deposition in the kidney at higher doses. In chronic studies, NOELs were about 410 mg/kg/d (male mice), 1215 mg/kg/d (female mice), 108 mg/kg/d (male rats) and 56 mg/kg/d (female rats), on the basis of an equivocal increase in epididymal microconcretions in male mice and depression of bodyweight gain in rats.

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Dogs were possibly more sensitive to the effects of halosulfuron than rodents. In a l-year PO study, the NOEL was considered to be 1 mg/kg/day for males and 10 mg/kg/day for females; body weight gains, cholesterol levels and lymphocyte values were decreased in males and red cell parameters were decreased in females at 40 mg/kg while at 10 mg/kg, body weight gains and cholesterol levels were decreased *in* males. There were no consistent indications of any particular target organ in the above studies.

In a PO rat teratology study (0, 75, 250 and 750 mg/kg), numbers of foetuses and litters with malformations (external, visceral and skeletal) were only increased at 750 mg/kg (3.1% and 27%, respectively) compared to control (0.6% and 8%); several visceral and skeletal variations were also increased at this dose. The NOEL for maternal and development toxicity was 250 mg/kg/day. There was no evidence of a teratogenic effect of halosulfuron in rabbits.

Halosulfuron was not carcinogenic (mice and rats) or genotoxic and did not affect fertility (rats).

Safety Directions

MONTURF is to be used for selective control of Nutgrass ('Cyperus rotundus') and Mullumbimby couch ('Cyperus brevifolius') in warm season turf. It is estimated that users will apply up to 0.1 kg ai/ha twice yearly; for a golf-course of 18 fairways, each of 1.5 ha, this would equate to a total of 5.4 kg halosulfuron per year. The major potential for exposure would be by dermal contact. After dispersal of the dry-flowable water dispersible granules and addition of 200 mL/100L of a 600 g/L non-ionic surfactant or equivalent (to ensure uptake of the active), application is by a boom spray, using flat nozzles. Proposed safety directions are as follows:-

221 161 162	Dust will irritate the eyes and skin
210 211	Avoid contact with eyes and skin
351	Wash hands after use

On the basis of slight skin and eye irritation with a dust (pulverised water-dispersible granules), it is suggested that 221 161 and 162 be used. However, since the risk from dermal exposure to dust and to the ai in a dilute spray is slight, it is considered that the requirement for gloves (290 and either 294 or 312 - 'wear elbow-length PVC gloves' or 'wear rubber gloves') is unnecessary.

Apart from the addition of 221 161 162, the above entry is almost equivalent to those for chlorsulfuron and sulfometuron.

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RECOMMENDATIONS

1. There are no objections, on the basis of toxicological considerations, to the approval of halosulfuron TGAC and registration of the end-use product, MONTURF Herbicide.
2. While the overall toxicity of halosulfuron was low, suggesting the possibility of an Appendix B entry, the small increase in fetal malformations in a rat PO teratology study (NOEL of 250 mg/kg/d) suggests that a Schedule 5 entry may be more appropriate.
3. The lowest NOEL of 1 mg/kg/d was established in a 1-year PO dog study; on the basis of safety factor of 100 (satisfactory data), an ADI of 0.01 may be set.
4. FIRST AID AND SAFETY DIRECTIONS

Appendix H, Part 2 -New Entry

Halosulfuron-methyl	DF	WG	750 g/kg	129	133	221	161	162
		or less		210	211	351		

Appendix E, Part 2 -New Entry

Halosulfuron-methyl ……..	a	770

The recommendations of the FASD Discussion Group were:

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SUMMARY OF TOXICOLOGICAL HAZARD

Date of Preparation: November 1993

Chemical name: Halosulfuron-methyl Worst oral L050 in rats: 7,758 mg/kg in female rats

Worst oral L050 in other species: 9,295 mg/kg in female mice

Worst dermal L050: >2,000 mg/kg in rats

Worst inhalation LC50: >6,000 mg/m3 in rats (4h, whole-body)

Skin irritation: None in rabbits

Eye irritation: Slight in rabbits

Skin sensitisation: None in guinea pigs

Remarks:

T-value: 770

NEL: 1 mg/kg in a 1-year oral (capsule) dog study

TES2-1789

SUMMARY OF TOXICOLOGICAL HAZARD

Date of Preparation: November 1993

Chemical name: Halosulfuron-methyl

These data were obtained with MON 12022, the powder equivalent of a 75% ai granule formulation.

Worst oral LD50 in rats: 1,287 mg/kg in rats

Worst oral LD50 in other species:

Worst dermal LD50: >5,000 mg/kg in rats

Worst inhalation LC50: >5,700 mg/kg in rats

Skin irritation: Slight in rabbits

Eye irritation: Slight in rabbits

Skin sensitisation: None in guinea pigs

Remarks:

T-value:

NEL:

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SUMMARY OF TOXICOLOGICAL HAZARD

Date of Preparation: November 1993

Chemical name: Halosulfuron-methyl

These data were obtained with MON 12051, the powder equivalent of a 50.5% ai granule formulation.

Worst oral LD50 in rats: 3,170 mg/kg in male rats

Worst oral LD50 in other species:

Worst dermal LD50: >5,000 mg/kg in rats

Worst inhalation LC50: >4,800 mg/kg in rats

Skin irritation: Slight in rabbits

Eye irritation: Moderate in rabbits

Skin sensitisation: None in guinea pigs

Remarks:

T-value:

NEL:

TES2-1789

HALOSULFURON-METHYL

Product: MONTURF Herbicide

Company: Monsanto Australia Limited

Submission no: 9937

Date: November 1993

1. INTRODUCTION

Halosulfuron-methyl (henceforth referred to as halosulfuron) is a new proprietary chemical from Nissan Chemical Industries Ltd to be marketed in Australia by Monsanto Australia Limited. It is a sulfonyl urea herbicide which is claimed to have unique post-emergent activity on 'Cyperus' spp and excellent safety on turf species. In Australia MONTURF is to be used for selective control of Nutgrass ('Cyperus rotundus'), and Mullumbimby couch ('Cyperus brevifolius') in warm season turf. This application is for TGAC clearance of the active, for poison scheduling and for approval of a 750 giL EUP, 'MONTURF' Herbicide for use on certain weeds in turf ie. this application is for non-crop use.

Chemistry of the TGAC

Common name: Halosulfuron methyl

Chemical name:

(i) IUPAC

Methyl 5-{[4, 6-dimethoxy-2-pyrimidinyl)amino]carbonyl-aminosulfonyl}-3-chloro-1-methyl-1-H-pyrazol-4-carboxylate

or

Methyl 3-chloro-5-(4, 6-dimethoxypyrimidin-2-ylcarbamoylsulfamoyl)-1-methylpyrazole-4-carboxylate

(ii) Chemical Abstracts

1H-pyrazole-4-carboxylic acid, 3-chloro-5-[[[[(4,6-dimethoxy-2-pyrimidinyl)amino]carbonyl]amino]sulfonyl]-1-methyl, methyl ester

(iii) CAS No. 100784-20-1

(iv) Distinguishing Name

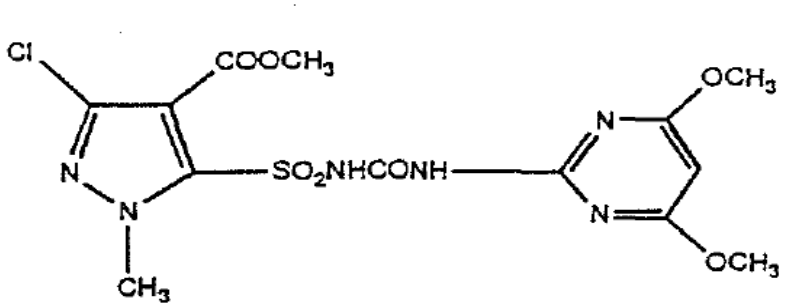
MONTURF Herbicide

(iv) Company Code Name

NC-319, MON 12000

TES2-1789

Structural Formula:



Empirical Formula: $C_{13}H_{15}N_6O_7SC1$

Molecular Wt: 434.82

Manufacturer: Nissan Chemical Industries Ltd
Kowa-Hitosubashi Building
7-1 Kanda-Nishiki-cho 3-chrome
Chiyoda-ku, Tokyo 101, Japan

Plant:

Onoda Plant, Nissan Chemical Industries Ltd
6903-1, Oaza Onoda
Onoda, Yamaguchi Pref. 756, Japan

Chemical and Physical Properties of TGAC

Colour: light white

Odour: odourless

Physical State: powdered solid

Melting Point: 175.5-177.2°C

Octanol/Water Partition

Coefficient (at 23°C): Kow = 47 at pH 5
Kow = 0.960 at pH 7
Kow = 0.290 at pH 9
Unstable in the aqueous layer at pH 9

Vapour Pressure: less than 1 x 10^{-7} mmHg at 25°C

Solubility (at 20°C):

methanol	1.616 g/L
n-hexane	0.013
water, pH 5	0.015
pH 7	1.65
pH 9	7.47 (24h)

pH 9	3.83 (48h)
pH 9	2.63 (72h)

(The change with time in solubility at pH 9 is indicative of instability.)

pH: 4.11 (1% w/v slurry at 25°C)

Density/Specific Gravity: 1.618 g/mL at 25°C

Oxidation Stability (air): not an oxidising or reducing agent

Dissociation Constants: K_a = 3.61 x 10-4 at 22.4°C

Hydrolysis: half-life =18h (pH 5)

= 14.5 days (pH 7)

= 27 days (pH 9)

Photostability: 75.8% loss in purity in sunlight (24h)

Declaration of Composition

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Chemistry of End-Use Product

CONFIDENTIAL

NOT FOR PUBLIC RELEASE

Chemical and Physical properties of the EUP

Colour: almond

Physical State: solid granules

Odour: scorched vanilla

pH (1% solution): 6.6 at 25°C

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2. METABOLISM AND TOXICOKINETICS

2.1 Absorption, Distribution, Excretion and Metabolism of Halosulfuron in Rats Southern Research Institute, Alabama.

Study no. MSL-11070. Date Dec. 1990 (GLP)

Using halosulfuron separately labelled with 14C in the pyrimidine and pyrazole rings (Pd- and Pz-14C-halosulfuron), groups of Sprague-Dawley rats were given single PO doses at 5 and 250 mg/kg

		14C-Pd			14C-Pz	
LD		HD	RD	LD	HD	RD
% Recovery of Dose						
(excreta, cage wash)	82	90	89	100	98	96

(in 1% aqueous Tween 80) while another group was given 14 daily unlabelled doses of 5 mg/kg halosulfuron followed by one 14C-labelled dose. The following amounts were recovered over 7 days:-

Data are means for male and female rats.

Most of the radioactivity appearing in the urine was eliminated within 12h, that in faeces within 2d. Regardless of the position of the label, approximately equal proportions were eliminated in faeces and urine. Regardless of the dose, number of doses or label position, females excreted somewhat less in urine than males but only slightly more in faeces; at 7 days, carcass residues in females were slightly higher than in males. There was no recovery of radioactivity in expired air after Pz-14C label and only 0.3% of the dose after Pd-14C-halosulfuron. Since no IV dosing or bile cannulation experiments were conducted, it is not possible to comment on the extent of PO absorption of halosulfuron in rats; from the above data, it would not be less than about 50%.

After 7 days the carcass contained less than 1% of the dose in the above experiments. Blood radioactivity was about 3x background at the high dose of Pd-14C-halosulfuron; all other tissues contained less than 2x background.

Most urinary metabolites possessed both the pyrimidine and pyrazole rings; little parent compound remained. Faecal metabolite profiles were similar to urine except faeces contained measurable levels of parent. There were no significant sex differences. A proposed metabolic pathway is shown in Fig. 1. The major metabolite was desmethyl-halosulfuron (50-70% of urinary radioactivity), then 5-hydroxydesmethyl-halosulfuron (tentatively identified) formed 20-40% of LD and repeat-dose urine, less at the HD probably because of saturation of this metabolic pathway. Minor metabolites included 4,6-dihydroxy-halosulfuron, N-demethyl-halosulfuron, halosulfuron acid (only at the HD; less than 5% of urinary metabolites), and 5-hydroxy-halosulfuron. Cleavage of the molecule to give separate ring metabolites represented only a minor metabolic pathway. There was less than 1% 3-C1-sulfonamide in urine.

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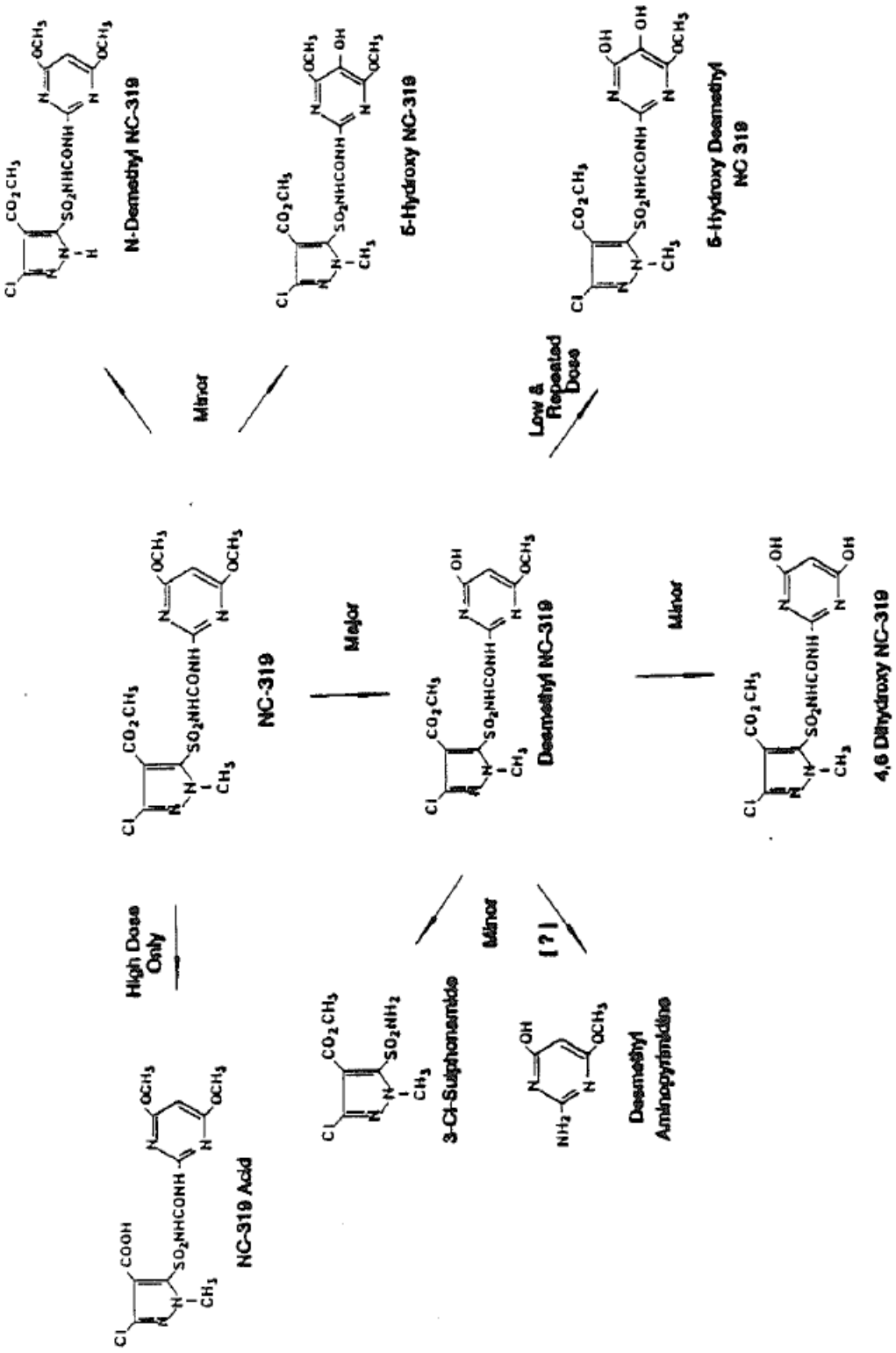
: Proposed Metabokic Pathway for Haosulfuron (NC-319) in Rats



2.2 Metabolism of Halosulfuron in Lactating Goats Hazleton Labs America, Inc. Study no. MSL-10660 Completion Date 21 Nov. 1991 (GLP)

Two lactating goats were given 20 mg/day by capsule (approx. equivalent to 11 ppm in the diet) of 14C-halosulfuron for 4 days; one received only pyrazole-labelled halosu1furon, the other a 50:50 mixture of pyrimidine and pyrazole-labelled halosulfuron. The animals were sacrificed 22h after the last dose. Total recoveries in the samples collected (urine, faeces, liver, kidneys, fat, muscle, blood, bile, GI tract and contents) were 95% and 99%. Urine had about 85% of the total dose, faeces approx. 12% and milk, less than 0.1%. The majority of radioactivity was eliminated within 24h of each daily dose. Concentrations in milk ranged from 0.003 to 0.021 ppm (halosulfuron equivs), muscle less than 0.002 ppm (detection limit), fat less than 0.01 ppm; liver and kidney were higher at 0.12-0.027 ppm. No differences in distribution were noted between labels. The majority of radioactivity in urine was unchanged halosulfuron. The major residue in tissues was halosulfuron. Desmethyl-halosulfuron and halosulfuron acid were detected, primarily in liver and kidney.

2.3 Metabolism of Halosulfuron in Laying Hens Hazleton Labs America, Inc. Study no. MSL-11578 & 10657 Completion Dates 1 March 1991 & May 1992 (GLP)

Laying hens (15) were given 14C-halosulfuron in capsules at 1.1 mg/day (equiv. to 10 ppm in the diet) for 4 days; 5 received only pyrazole-labelled halosulfuron, the others a 50:50 mixture of pyrimidine and pyrazole-labelled halosulfuron. The animals were sacrificed 22h after the last dose. Eggs were collected 2x/day and hens were killed 22h after the last dose. The majority of radioactivity (95%) was in excreta, mostly excreted within 24h of each dose. Eggs and other tissues contained 0.2% and 0.5% of the total dose. Concentrations in tissues were: egg white (0.006-0.064 ppm); yolk (0.008-0.057 ppm); and liver (0.125-0.196 ppm). No differences in results were apparent between the labels. Major radioactive components of excreta were halosulfuron and 5-hydroxy-halosulfuron.

3. ACUTE STUDIES

The following studies were conducted according to GLP guidelines.

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Study Type	Species	Outcome	Reference
ACTIVE INGREDIENT			
Oral	Mouse (CD-1)	LD50 = 16,156 mg/kg (m)	
		LD50 = 9,295 mg/kg (f)	
		LD50 = 11,173 mg/kg (m & f)	(1)
Oral	Rat (SD)	LD50 = 10,435 mg/kg (m)	
		LD50 = 7,758 mg/kg (f)	
		LD50 = 8,866 mg/kg (m & f)	(2)
Intra-peritoneal	Mouse (CD-1)	LD50 = 1,215 mg/kg (m)	
		LD50 = 1,226 mg/kg (f)	
		LD50 = 1,228 mg/kg (m & f)	(3)
Intra-peritoneal	Rat (SD)	LD50 = 1,463 mg/kg (m)	
		LD50 = 1,164 mg/kg (f)	
		LD50 = 1,293 mg/kg (m & f)	(4)
Subcutaneous	Mouse (CD-1)	LD50 > 10,000 mg/kg (m & f)	(5)
Subcutaneous	Rat (SD)	LD50 = 3,365 mg/kg (m)	
		LD50 = 3,247 mg/kg (f)	
		LD50 = 3,289 mg/kg (m & f)	(6)
Dermal	Rat (SD)	LD50 > 2,000 mg/k~	(7)
Inhalation	Rat (SD)	LC50 > 6,000 mg/m (m & f)	(8)
Eye Irritation	Rabbit (NZ)	slight eye irritant	(9)
		not an eye irritant	(10)
Skin Irritation	Rabbit (NZ)	not a skin irritant	(11)
Skin Sensitis'n	Guinea Pig (DH)	not a skin sensitiser	(12)
END-USE PRODUCT	(MON 12022)		
Oral	Rat (SD)	LD50 = 1,287 mg/kg (m & f)	(13)
Dermal	Rat (SD)	LD50 > 5,000 mg/k~ (m & f)	(14)
Inhalation	Rat (SD)	LC50 > 5,700 mg/m (m & f)	(15)
Eye Irritation	Rabbit (NZ)	slight eye irritant	(16)
Skin Irritation	Rabbit (NZ)	slight skin irritant	(17)
Skin Sensitis'n	Guinea Pig (DH)	not a skin sensitiser	(18)
END-USE PRODUCT	(MON 12051)		
Oral	Rat (SD)	LD50 = 3,170 mg/kg (m)	
		LD50 > 6,000 mg/kg (f)	
		LD50 = 4,074 mg/kg (m & f)	(19)
Dermal	Rat (SD)	LD50 > 5,000 mg/k~ (m & f)	(20)
Inhalation	Rat (SD)	LC50 > 4,800 mg/m (m & f)	(21)

Eye Irritation	Rabbit (NZ)	moderate eye irritant	(22)
Skin Irritation	Rabbit (NZ)	slight skin irritant	(23)
Skin Sensitis'n	Guinea Pig (DH)	not a skin sensitiser	(24)

MON 12022 is the powder equivalent of MON 12037 which is MONTURF Herbicide, the granular formulation of halosulfuron-methyl to be used in Australia; MON 12022 contains 75% ai.

MON 12051 is the powder equivalent of MON 12088 which is a granular formulation of halosulfuron-methyl; MON 12051 contains approximately 50.5% ai.

SD = Sprague Dawley: NZ = New Zealand White: DH = Dunkin-Hartley

These acute toxicity studies were conducted in the following laboratories:-

Study no. Prefix	Laboratory
HL	Hazleton Laboratories America Inc. Vienna, Virginia, USA
ML	Monsanto Agricultural Company Environmental Health laboratory St Louis, Missouri, USA
BD	Bio/dynamics Inc. Millstone, New Jersey, USA
HF	Hazleton-IFT Les Oncins, BP 118 69210 L'Arbresle, France
SB	Springborn Laboratories Inc. Life Sciences Division Spencerville, Ohio 45887, USA

Dates given are study completion dates·.

ACTIVE INGREDIENT

(1) Acute Oral Study in Mice (Study HL-89-334; 18 Aug. 1988)

Fasted Crl:CD-1(ICR)BR mice (10/sex/gp) were given halosulfuron (98.5%) in 0.5% CMC by gavage at 4000, 5000, 7500 and 10000 mg/kg and observed for 14 days. Deaths occurred within the first 2 days. Clinical signs included depression, ataxia, urine staining, tremors and, in 1/10 HD females, convulsions. Gross pathology findings involved lungs, liver and spleen (discoloration) and stomach and intestines (discoloration, abnormal contents, distension, and thin walls). All surviving mice appeared normal by day 3 and gained wt until termination.

(2) Acute Oral Toxicity in Rats (Study HL-89-317; 23 May, 1990)

Fasted Sprague Dawley rats (10/sex/gp) were given halosulfuron (lot 319T8702) in 0.5% CMC by gavage at 4000, 5000, 7500 and 10000 mg/kg and observed for 14 days. Deaths occurred within the first 4 days. Clinical signs included depression, ataxia, urine staining, soft faeces, hunched posture, and, in a few animals, tremors. Gross pathology findings involved lungs, liver, kidney and spleen (discoloration) and stomach and intestines (discoloration,

abnormal contents, distension). All surviving rats appeared normal by day 8 and gained wt until termination.

(3) Acute Intra-peritoneal Toxicity in Mice (Study HL-89-335; 9 Dec. 1988)

Fasted Crl:CD-1(ICR)BR mice (10/sex/gp) were given halosulfuron (98.5%) in 0.5% CMC/O.1% Tween 80 by IP injection at 500, 1000,

1250 and 2000 mg/kg and observed for 14 days. Deaths occurred within the first day. Clinical signs included depression, ataxia, rough coat, laboured respiration, tremors and, at the HD, convulsions. No gross pathology findings were observed. Apart from rough coat at the HD, surviving mice appeared normal by day 2 and gained wt until termination.

(4) Acute Intra-peritoneal Toxicity in Rats (Study HL-89-336; 9 Dec. 1988)

Fasted SD rats (10/sex/gp) were given halosulfuron (98.5%) in 0.5% CMC/O.1% Tween 80 by IP injection at 500, 1000, 1500, 1750 and 2000 mg/kg and observed for 14 days. Deaths occurred within the first day. Clinical signs included depression, ataxia, laboured respiration, tremors and, at the HD, convulsions. Gross pathology findings included abnormal contents in the abdominal cavity (dead animals only) and discoloration of the lungs, liver, spleen and kidney (dead animals of 1000 mg/kg gp). Surviving rats appeared normal by day 2 and gained wt until termination.

(5) Acute Subcutaneous Toxicity in Mice (Study HL-89-329; 7 March 1989)

Crl:CD-1(ICR)BR mice (10sex/gp) were given halosulfuron (98.5%) in 0.5% CMC/0.1% Tween 80 by SC injection at 5000, 7500, and 10000 mg/kg and observed for 14 days. Deaths which occurred were within the first day; mortality rates were 5, 35 and 15%. Clinical signs included depression, ataxia, rough coat, laboured respiration, and tremors. Gross pathology findings were noted in lungs, liver and spleen (discoloration) and intestines (thin walls, abnormal contents). At the HD, 16/17 surviving mice gained wt until termination.

(6) Acute Subcutaneous Toxicity in Rats (Study HL-89-337; 9 Dec. 1988)

SD rats (10/sex/gp) were given halosulfuron (98.5%) in 0.5% CMC/0.1% Tween 80 by SC injection at 1000, 2500, 4000 and 6000 mg/kg and observed for 14 days. Mortality rates were 0, 35, 80 and 90%. Deaths occurred within the first 3 days, the majority on the first day. Clinical signs included depression,ataxia, laboured respiration, Red stains on nose/eyes, tremors and soft faeces. Gross pathology findings were noted in the stomach and intestines (abnormal contents, distension, thin walls), the lungs, liver, spleen, thymus, adrenals and kidney (discoloration) the uterus (distension) and the injection site (alopecia, necrosis, swelling).

(7) Acute Dermal Toxicity in Rats (Study HL-89-325; 23 May 1990)

Halosulfuron (98.5%) was applied to a 1.5-inch square gauze pad and applied to the moistened skin (clipped backs) of Sprague Dawley CD rats (10/sex) at a dose of 2000 mg/kg, with observation for 14 days. There were no clinical observations or gross lesions and all animals survived and gained wt.

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(8) Acute Inhalation Toxicity in Rats (Study ML-91-140; 18 Sept. 1991)

SD rats (5/sex/dose) were exposed for 4h (whole body) to an atmosphere containing 6000 mg/m of halosulfuron dust (99.7% pure, milled to reduce the Mass Median Aerodynamic Diameter (MMAD) 66% to 9.4 microns; MMAD ± GSD = 4.3 ± 2.2 microns), with 14 days observation followed by gross pathology. All animals survived and increased weight. Immediate clinical signs in several animals included hypoactivity, laboured respiration, red/pink nasal discharge, perioral wetness and encrustation, with red/brown perinasal encrustation in some on days 1 and 2. Necropsy findings were negative.

(9) Eye Irritation in Rabbits (Study BD-91-130; 14 June 1991)

Halosulfuron (99.3%; 0.1 mL, 58 mg) was placed in the right eyes of NZ White rabbits (3/sex), followed by a 3-day observation period. Slight to moderate irritation (redness, chemosis, discharge) was seen, recovered within 24h. No corneal effects were seen while 2 had iridial changes only at 2h.

(10) Eye Irritation in Rabbits (Study HF-89-328; 3 May 1990)

Halosulfuron (98.5%; 92 mg) was placed in the right eyes of NZ White rabbits (6 males), followed by a 3-day observation period. Slight chemosis was seen at 24h, recovered within 48h. No opacities were seen while iridial congestion was seen, largely recovered by 72h. According to EC classification (Directive 83/467) it was classified as a non-irritant.

(11) Skin Irritation in Rabbits (Study HF-89-327; 3 May 1990)

Halosulfuron (98.5%) was applied as a paste (0.5g in 0.2lg water) unde2 semi-occlusive dressing to clipped intact skin (approx. 6 cm^2) of NZ White rabbits (6 males) for at least 4h, with observation for 14 days. No corrosion or irritation was observed.

(12) Skin Sensitisation in Guinea Pigs (Study HF-89-326; 27 April 1990)

Halosulfuron (98.5%) was tested in Dunkin Hartley guinea pigs (10/sex) according to the protocol of Magnusson and Kligman, with DNCB as a positive control. There was no reaction with the test compound indicating any cutaneous intolerance or sensitisation.

END-USE PRODUCT (MON 12022)

MON 12022 is the powder equivalent of MON 12037, a granular 75% formulation which is claimed to be the same as the proposed Australian EUP.

(13) Acute Oral Toxicity in Rats (Study BD-92-115; 13 May 1992)

MON 12022 was given by gavage (in dist. water) at 1056, 1500 and 2130 mg/kg to fasted CD rats (5/sex/gp). The most notable clinical signs were lethargy and yellow anogenital staining, with

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mortalities of 20, 80 and 90% respectively. Gross pathology of animals which died revealed discoloration of nasal turbinates and lungs.

(14) Acute Dermal Toxicity in Rats (Study BD-92-115; 14 May 1992)

MON 12022 was applied on gauze (saline moistened) under occlusion to shaved backs of CD rats (5/sex/gp) for 24h at 5000 mg/kg. Signs included yellow anogenital staining and chromodacryorrhea. Superficial necrosis was observed in all animals between days 1-4 post-treatment. No internal abnormalities were noted.

(15) Acute Inhalational Toxicity in Rats (Study ML-92-130j 17 April 1992)

Sprague-Dawley rats (5/sex) were exposed for 4h (whole body) to MON 12022 dust, then observed for 14 days. The MMAD of particles was 3.8 μm; 91% and 4% of particles wee less than 10 and 1 pm respectively. 3The time-weighted average analytical concentration was 5,700 mg/m^3. There were no deaths. Clinical signs included laboured respiration, peri-ocular wetness, clear nasal discharge, perioral wetness and deposition of material on the skin. Red/brown perinasal encrustation was seen on days 1 and 2 but animals appeared normal from then on, with no gross necropsy findings.

(16) Eye Irritation in Rabbits (Study BD-92-115; 4 May 1992)

Slight to moderate conjunctival irritation, including redness, swelling and discharge was observed when 28 mg (approx. 0.1 mL) of MON 12022 was placed in the eyes of 6 NZ White rabbits. One of 6 showed corneal epithelial ulceration and iridial changes through 24h but all eyes were clear on or before day 7.

(17) Skin Irritation in Rabbits (Study BD-92-115; 23 April 1992)

Very slight erythema with no or slight oedema was noted when 0.5g of MON 12022, moistened with saline, was applied to the clipped backs of NZ White rabbits (3/sex) for 4h (under occlusive dressing). All were free of dermal irritation by 10 days.

(18) Skin Sensitisation in Guinea Pigs (Study BD-92-116; 23 April1992)

MON 12022 was tested in Dunkin Hartley Hra: (DH)BR guinea pigs (3/sex in a range-finding study, then 5/sex for the sensitisation study and 57sex for the irritation controls), according to a modified protocol of Buehler. There was no reaction with the test compound indicating any dermal sensitisation. Concurrent positive controls were not conducted but historical data on DNCB was presented.

END-USE PRODUCT (MON 12051)

MON 12051 is the powder equivalent of a granular formulation of halosulfuron and contains approx. 50.5% ai.

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(19) Acute Oral Toxicity in Rats (Study SB-91-45; 12 June 1991)

MON 12051 was administered to fasted CD rats by gavage (in dist. water). In females (5/gp) given 5000 and 6000 mg/kg, mortalities were 20 and 40%. At 2000, 4000 and 5000 mg/kg in males (5/sex/gp), mortalities were 0, 100 and 80%. Clinical signs included salivation, breathing abnormalities, decreased activity, wobbly gait, decreased defecation, soft stools, urine stains, and dark material on the face. Gross necropsies were negative.

(20) Acute Dermal Toxicity in Rats (Study SB-91-45; 12 June 1991)

MON 12051 was applied on gauze (saline moistened) under occlusion to shaved backs of CD rats (5/sex/gp) for 24h at 5000 mg/kg. There were no mortalities. Signs included yellow anogenital staining, dark material around the face, decreased defecation and dermal irritation at the test site. No internal abnormalities were noted.

(21) Acute Inhalational Toxicity in Rats (Study ML-91-13; 15 March 1991)

Sprague-Dawley rats (5/sex/gp) were exposed for 4h (whole body) to MON 12051 dust at nominal concentrations of 10000 and 13000 mg/m^3, then observed for 14 days. The MMAD of particles was 3.8 μm; 91% and 4% of particles were less than 10 and 1 μm respectively. Time-weighted average analytical concentrations were 4200 and 4800 mg/$m^{3.}$ One male at the higher dose died on day 1 after exposure. Clinical signs included urine-stained hair, peri-ocular wetness, clear nasal discharge, perioral wetness and deposition of material on the skin. Red/brown perinasal encrustation was seen up to day 3 post-exposure but animals appeared normal from then on, with no gross necropsy findings. All animals initially lost wt but then gained wt from day 2 post-exposure.

(22) Eye Irritation in Rabbits (Study SB-91-45; 12 June 1991)

Slight to moderate conjunctival irritation, including redness, swelling and discharge was observed when 3 7 mg (approx. 0.1 mL) of MON 12051 was placed in the eyes of 6 NZ White rabbits. Corneal opacity was noted in 3/6 at 24h, clearing on or before day 3. All eyes were clear on or before day 7.

(23) Skin Irritation in Rabbits (Study SB-91-45; 12 June 1991)

Very slight to slight dermal irritation (slight to well-defined erythema with slight oedema) was noted when 0.5g of MON 12051, moistened with saline, was applied to the clipped backs of NZ White rabbits (3/sex) for 4h (under occlusive dressing). All were free of dermal irritation by 7 days.

(24) Skin Sensitisation in Guinea Pigs (Study SB-91-46; 19 June 1991)

MON 12051 was tested in Hartley-derived guinea pigs (2/sex in a range-finding study, then 5/sex for the sensitisation study and 5/sex for the irritation controls), according to a modified

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protocol of Buehler. There was no reaction with the test compound indicating any dermal sensitisation. Concurrent positive controls were not conducted but historical data on DNCB was presented.

4. SHORT TERM REPEAT DOSE STUDIES

4.1 28-Day Dietary Study in Mice Hazleton Labs America, Inc.

Study no. HL-89-314. Report Date 17-Aug-1988 (GLP)

Halosulfuron (98.5%) was administered in the feed to Crl: CD-1(ICR)BR mice (10/sex/gp) at levels of 0, 300, 1000, 3000 and 10000 ppm for 28 days.

Severe depression of bodywt gain was seen at the HD (males and females 45 and 32% below control bodywts respectively), less so at 3000 ppm (29 and 26% below control males and females). Otherwise there were no clinical signs and neither survival nor food intake were affected. Ophthalmoscopy was negative, as was haematology and clinical chemistry. At the HD, relative liver wts were increased (15% in males, 18% in females). Gross pathological examination revealed centrilobular hypertrophy, increased vacuolation and a slight increase in focal coagulative necrosis in HD males. 2/10 HD males had alveolar/bronchiolar adenomas (typical of those found in CD-1 mice) and 1/10 HD females had an ovarian choriocarcinoma. No compound-related effects were noted at 1000 ppm (about 150 mg/kg) and below.

4.2 28-Day Dietary Study in Rats Hazleton Labs America, Inc.

Study no. HL-89-315. Report Date 17-Aug-1988 (GLP) Halosulfuron (98.5%) was administered in the feed to Sprague Dawley rats (10/sex/gp) at levels of 0, 300, 1000, 3000 and 10000 ppm for 28 days.

Depression of bodywt gain was seen at the HD (males and females 20 and 35% below control bodywts respectively), less so at 3000 ppm (females 18% below controls). Otherwise there were no clinical signs and neither survival nor food intake were significantly affected. Ophthalmoscopy was negative, as were urinalyses. Haematology revealed a slight increase in Hct and Hb while clinical chemistry noted slightly-decreased total protein, albumin, globulin and glucose. Relative wts of kidneys in HD females and relative wts of livers in HD males were increased. Gross pathological examination was negative. Histopathology revealed an equivocal increase in liver vacuolation in HD females and an increase in individual cell degeneration/necrosis in the pancreas of 3000 and 10000 ppm animals. No compound-related effects were noted at 1000 ppm (about 100 mg/kg) and below.

In this study, no effects were noted at 1000 ppm (approx. 100 mg/kg/d) with reduced bodywt gain and some pancreatic cell pathology at the next highest dose.

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4.3 5-Day Pilot Dermal Study in Rats Hazleton Labs America,Inc.

Study no. HL-89-319. Report Date 3-0ct-1989 (GLP)

This study was designed to assist in the selection of dose levels for a subsequent 21-day dermal toxicity study. Halosulfuron (99.1%) was dermally applied to Sprague-Dawley rats (5/sex/group) at levels of 0, 10, 100, 500 or 1000 mg/kg/day; application was to shaved trunk

Two females at 100 mg/kg/day died on the 4th day of dosing. At necropsy, both animals were noted to have mottled lungs, suggested to be a post-mortem autolytic change. There were no gross necropsy findings attributed to treatment in surviving animals.

Clinical observations noted in all treatment groups (including controls) were bloody crust on the nose, chromodacryorrhea, and lacrimation. There was an isolated incidence of soft faeces in one HD male, as well as an observation of sores in a 500 mg/kg male which was attributed to the cardboard collars (used to prevent oral compound intake as a result of grooming).

Mean body weights of 500 mg/kg males and 1000 mg/kg females were significantly depressed. There were no noteworthy changes in food consumption in any of the treatment groups. It may be concluded that dermal administration of up to 1000 mg/kg/day of halosulfuron to Sprague-Dawley rats did not result in any clinical observations and/or gross necropsy findings suggestive

of a test-material effect.

4.4 21-Day Dermal Study in Rats Hazleton Labs America, Inc.

Study no. HL-89-339 Report Date 10-Jan-1990 (GLP)

Halosulfuron (99.1%) was applied to the skin of Sprague-Dawley rats (5/sex/group) at dose levels of 0, 10, 100 or 1000 mg/kg/day for 21 consecutive days; application was to shaved trunk skin (approx. 10% of body surface) on occluded, saline-dampened gauze pads.

One 100 mg/kg female was found dead on Day 14. Gross necropsy revealed changes in the kidney and liver but not severe enough to result in the death of the animal. All other rats survived until scheduled sacrifice. Statistical evaluation of body weight, food consumption, serum chemistry, and organ weight data failed to reveal any significant differences between treated groups and their respective controls. Evaluation of haematology values revealed significantly increased HD male haemoglobin and a significant increase in 100 and 1000 mg/kg haematocrit when compared to respective mean controls. This alteration was ascribed in the report to a mild state of dehydration, possibly associated with the stress related to the physical administration of the test material.

Gross and microscopic examinations of tissues revealed a number of alterations which were considered to be incidental to treatment.

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It may be concluded from this study that halosulfuron caused few noteworthy signs of toxicity when administered dermally to rats for 21 consecutive days at doses up to 1000 mg/kg/day.

4.5 Oral (Capsule) Maximum Tolerated Dose Study in Dogs

Hazleton UK. Study no. HK-89-316. Report Date Aug. 1988 (GLP)

This study was divided into two phases. The first phase was used to determine a minimum lethal dose of halosulfuron. The second phase evaluated the toxicity of halosulfuron (98.5%) when given as a repeated dose for 14 days.

In the first phase, purebred beagle dogs (1/sex) received the test article in gelatine capsules according to the following schedule:

Days	Dose level (mg/kg/day)
1 to 4	50
5 to 8	100
9 to 12	200
13 to 16	400
17	800

One male and one female received gelatine capsules alone and served as controls.

Doses of 50 to 400 mg/kg/day did not affect body weights or cause any clinical effects which could be related to treatment. Within 3 hours after 800 mg/kg, both animals became sluggish and subdued, ultimately were unable to walk and had body tremors; both were sacrificed after 5h.

In the second phase, dogs (l/sex) received halosulfuron in gelatine capsules at 400 mg/kg/day for 2 days. This level proved to be too high for repeated administration, causing death of the male. Following a recovery period of 10 days, the female received 200 mg/kg/day for 14 days.

The male was killed approximately 6h after the second dose at 400 mg/kg. Prior to sacrifice, it was unsteady, with periods of muscular spasm and increased salivation. The female dog vomited after each of the two treatments at 400 mg/kg but showed no clinical abnormalities in the 10-day recovery period. The female vomited following the first dose of 200 mg/kg but not at

any dosing thereafter for 14 days. No treatment-related clinical signs or effects on body weight or food consumption were observed at 200 mg/kg.

In the single animal at 200 mg/kg, haemoglobin, red blood cell count and packed cell volume were slightly lower than predose values following 14 days of treatment, but were within normal values and were considered of equivocal toxicological significance. The female at 200 mg/kg also had slightly higher blood urea nitrogen and lower cholesterol levels than at predose.

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There was no gross pathology attributed to treatment with halosulfuron. The microscopic appearance of the bone marrow was normal.

In conclusion, when doses of halosulfuron were gradually increased up to 400 mg/kg/day in dogs, no treatment-related effects were observed. A single dose of 800 mg/kg was near-lethal to both dogs tested. A tolerance to halosulfuron may develop, however, as 400 mg/kg was severely toxic to one compound-naive animal. A female dog given 200 mg/kg/day for 14 days showed no treatment related effects in clinical observations, body weight, food consumption, gross pathology and histopathology of the bone marrow. The only changes observed were small variations in BUN and cholesterol levels.

5. SUBCHRONIC STUDIES

5.1 13-Week Dietary Study in Mice Hazleton Labs America, Inc.

Study no. HL-89-340 Report Date 27-April-1990 (GLP)

This range-finding study was designed to assist in the dose selection of dose levels for a subsequent oncogenicity study in mice. Halosulfuron (98.7%) was administered in the diet to CD-1 mice (20/sex/group) at doses of 0, 350, 2100, 3500 or 7000 ppm for at least 13 weeks.

One 3500 ppm male was found dead during week 9. Histological examination suggested that death was of a traumatic origin and apparently not compound-related. There was no other deaths nor any clinical observations suggestive of a compound effect. There was a significant depression in the HD male mean absolute body weights at week 13 and in mean body weight gains for weeks 0-13. There were no corresponding changes in food consumption. Mean clinical pathology values revealed a significant depression in HD male white blood cell, corrected white blood cell and lymphocyte values, and a significant increase in the HD female haemoglobin. No apparent changes were noted in serum chemistry values nor in ophthalmoscopic or gross necropsy examinations. Evaluation of organ weights revealed a significant increase in HD male mean relative organ wt of liver. Histological examination revealed a low incidence of thymic lymphocytolysis in HD females and a low incidence of reticuloendothelial hyperplasia in various

lymph nodes of HD females. The biological and/or toxicological significance of these findings is doubtful in view of the relatively low incidence of these lesions.

The NOEL for halosulfuron administered in the diet for at least 91 days to CD-1 mice was 3500 ppm (approx. 500 mg/kg/d).

5.2 13-Week Dietary Study in Mice (with 6-Week Recovery Period)

Inveresk Research International Limited, Scotland. Study no. IN-89-323. Report Date April 1990, Study Completion Date 25 Aug. 1988 (GLP)

CD-1 mice (10/sex/group) were dosed with halosulfuron (batch 319T8702) in the diet, at levels of 0, 100, 400, 1600 and 6400 ppm for 13 weeks. A further 10/sex were included in the control

and HD groups in order to determine the reversibility of any effects and kept for a 6-week recovery period.

One HD male died during bleeding in week 19; this was not considered to be due to dosing. There were no clinical signs and no intergroup body weight differences which could be attributed to compound intake. There were no notable intergroup differences in food or water consumption. Ophthalmoscopy was negative.

There were no notable intergroup differences in weeks 13 or 19, in either haematological or clinical chemistry parameters. There were no organ weight changes that could be attributed to halosulfuron in weeks 13 or 19, nor were there any intergroup differences in gross pathology findings. Histopathological changes were of the type and severity expected in mice of this age. Changes seen were mild and were not treatment-related. There were no significant findings after 6-weeks recovery.

In conclusion, dosing CD-1 mice with halosulfuron via the diet for 13 weeks produced no signs of toxicity. The NOEL was in excess of 6400 ppm (males: 937-1506 mg/kg/day; females: 1203-2032 mg/kg/day).

5.3 13-Week Dietary Study in Rats Inveresk Research

International Limited, Scotland. Study no. IN-89-320. Report Date Feb. 1990, Study Completion Date 14 June 1988 (GLP)

Sprague-Dawley rats (20/sex/group) were fed halosulfuron (batch 319T8702) in the diet at 0, 100, 400, 1600 or 6400 ppm for 13 weeks.

One female receiving 100 ppm died during week 10 of the study. Otherwise, there were no clinical signs which could be attributed to administration of halosulfuron. Animals receiving 6400 ppm showed a reduction in body weight gain compared to controls. HD females showed a slight reduction in food consumption and food utilisation efficiency. Ophthalmoscopy was negative.

There were no notable intergroup differences in mean haematological parameters. In HD males, cholesterol and total bilirubin levels were reduced and ALT was slightly increased. In HD females, cholesterol and total bilirubin were reduced. Urinalyses were negative.

In HD animals there were intergroup differences in absolute organ weights but these changes were not evident after adjustment for final body weight. There were no gross necropsy findings which could be attributed to halosulfuron. The only histopathological finding was an increased incidence of haemosiderin pigmentation in the tubular epithelium of the kidney. There was no

effect on kidney function and the increased incidence was limited to the 1600 and 6400 ppm groups. The NOEL was 400 ppm (males 28.8 mg/kg/day, females 37.3 mg/kg/day).

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5.4 13-Week Oral (Capsule) Study in Dogs Hazleton UK. Study no. HL-89-338 Report Date May 1991 (GLP)

Halosulfuron (98.5%) was administered in capsules to pure-bred beagles (4/sex/group) at dose levels of 0, 2.5, 10, 40 and 160 mg/kg/day for 13 weeks.

All animals survived. There were no clinical observations which were considered to be related to treatment. Body weight gains were depressed 20% in males and 41% in females at the HD and 10% in males and 27% in females at 40 mg/kg. Body weight gains in the other treatment groups of both sexes were similar to controls. Food consumption was not affected. Ophthalmoscopy was negative.

Haemoglobin, packed cell volume and RBC count were lower at week 13 for HD females. HD male white blood cell counts were 33% lower than controls at week 13. White blood cell counts were slightly reduced in the other male treatment groups, but values were within the historical control range and changes were not dose-related; thus the differences in WBC counts noted below the HD were not considered treatment related. (In a one-year capsule study in dogs (Study no. HL-89-343) in which halosulfuron was given at levels up to 40 mg/kg, no effect on WBC counts was noted at any time viz. 13, 26 or 52 weeks.) Cholesterol was moderately lower in HD animals and slightly lower in 40 mg/kg males. Total protein and albumin were slightly decreased in HD animals. There were no treatment-related effects on urinalysis parameters.

Relative liver weights were moderately increased in both sexes at the HD, and slightly increased in both sexes at 40 mg/kg and in females at 10 mg/kg. There were no treatment-related effects observed in gross or microscopic pathology. In the absence of any histopathological effects on the liver, the slight liver weight changes observed at 10 and 40 mg/kg were not considered to be toxicologically significant. In the one year study in dogs (Monsanto Study no. HL-89-343), no effect on liver weights were observed at dose levels up to 40 mg/kg.

In conclusion, the NOEL was considered to be 10 mg/kg/day.

6. CHRONIC STUDIES

6.1 18-Month Dietary Oncogenicity Study in Mice Hazleton Washington, Inc. Study no.

HL- 89-344 Report Date 29 Sept. 1992 (GLP)

Halosulfuron (98.7%) was administered in the diet to Charles River CD-1 mice (75/sex/gp) at target concentrations of 0, 30, 300, 3000 and 7000 ppm for 18 months. The upper dose of 7000 ppm was discussed with the EPA prior to study start, and represents the limit dose of 1 g/kg according to EPA's position paper on the maximum tolerated dose (EPA, 1987; NTIS Publication PB88-116736). Ten animals/sex/group were sacrificed at week 26, 15/sex/group

during weeks 53/54, and all survivors were sacrificed at weeks 79/80. All animals underwent gross and microscopic examination.

Serum samples were taken at the second interim sacrifice from 10 animals/sex (randomly selected across all dose groups) to assay for Mouse Hepatitis Virus (MHV). The following organs were weighed from 10 animals/sex/gp at each scheduled sacrifice; adrenals, brain (with brainstem), kidneys, liver (with gallbladder), seminal vesicles, spleen, testes (with epididymides) and thyroid/parathyroid.

Mean overall compound intakes were 0, 4.0, 41.1, 410.0 and 971.9 mg/kg/d (males) and 0, 5.2, 51.0, 509.1 and 1214.6 mg/kg/d (females).

There were no treatment-related effects on survival, clinical signs, body weights or food consumption. There were no gross pathology changes or organ weight changes considered treatment related. At terminal sacrifice, the number of males with microconcretions within the epididymal tubules were 0, 0, 0, 1 and 5 for the controls to HD, respectively. Epididymal microconcretions have been observed historically in control animals at Hazleton with a range of 0 to 2 out of 50-59 animals. The study pathologist concluded that the biological significance of these small focal lesions was questionable at both 3000 and 7000 ppm, and concluded that 7000 ppm was the NOEL. However, the incidence of five at the HD is statistically significant, outside of historical control range; overall it was inconclusive as to whether it is related to treatment.

Chronic active inflammation of the liver, typical of that seen with mouse hepatitis infection (confirmed by positive antibody titres to MHV), was noted in all treatment groups, with no treatment-related pattern at the second interim and terminal sacrifices. The presence of the liver lesions did not interfere with the morphological evaluation of the liver and the possible MHV infection did not compromise the study; survival in all groups was equal to or greater than historical controls, and absolute and relative liver weights for all groups at necropsy intervals were typical for mice at a comparable age.

There was no treatment-related increase in the incidence of any neoplasms.

In conclusion, the only evidence of toxicity was an equivocal increase in incidence of epididymal microconcretions in high dose males. The NOEL for chronic effects was at least 3000 ppm (410 mg/kg) in males and 7000 ppm (1214.6 mg/kg) in females.

6.2 2-Year Dietary Combined Chronic and Oncogenicity Study in Rats Hazleton Washington, Inc. Study no. HL-89-341 Report Date 29 Oct. 1992 (GLP)

Halosulfuron (98.7%) was administered in the diet to Charles River Sprague-Dawley (Crl:CDBR) rats (85/sex/gp) at target concentrations of 0,10, 100, 1000 and 2500 ppm for 24 months; a sixth group of 85 males received 5000 ppm. The upper dose was chosen in consultation with the

EPA prior to study start, and met the requirements specified in the EPA's position paper (EPA, 1987; NTIS Publication PB88-116736) on the maximum tolerated dose

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(MTD). Ten animals/sex/group were sacrificed at 6, 12 and 18 months, and all survivors were sacrificed at 24 months. All animals underwent gross and microscopic examination. The following organs were weighed from 10 animals/sex/group at each interim sacrifice, and from all surviving animals at the terminal sacrifice; adrenals, brain with brainstem, kidneys, liver, seminal vesicles, spleen, testes (with epididymides) and thyroid/parathyroid.

Mean overall compound consumption was 0, 0.44, 4.4, 43.8, 108.3 and 225.2 mg/kg/d (males) and 0, 0.56, 5.6, 56.3 and 138.6 mg/kg/d (females) in the respective groups (note that there was no female 5000 ppm group).

There were no treatment-related effects on survival or on clinical signs; survival was reduced at 1000 ppm in males but since there were no significant effects at the two highest doses, the finding was of questionable significance. In HD males, overall weight gain was 25% below controls. Overall body weight gain in all female treated groups was similar to control. However, body weight gain in HD females was 23, 33 and 19% less than control during weeks 13-24, 24-52 and 52-76, respectively. Body weight gain in HD females was similar to control during the weeks prior to week 13 and after week 76. The sustained suppression of body weight gain between weeks 13-76 was considered a treatment-related effect. There were no effects on food consumption.

Ophthalmoscopy was negative. There were no treatment-related effects on haematology, clinical chemistry or urinalysis. Organ weight analysis and gross pathological examinations did not reveal any treatment-related changes.

The incidence of seminal vesicle atrophy in males was 11/84, 15/82, 12/80, 17/84, 20/82 and 26/81 for the control to HD groups, respectively. However, its relationship to halosulfuron administration was questionable because no other associated pathology such as cell necrosis or inflammation was evident. Seminal vesicle atrophy has been reported to be a non-specific finding, often associated with chronic debilitating disease resulting from spontaneous causes such as neoplasia, chronic progressive nephropathy, or other genitourinary lesions. There were no other histopathological findings considered to be related to treatment. There was no evidence of any treatment-related increases in the incidence of any benign or malignant neoplasias.

In conclusion, the only evidence of toxicity was a body weight gain depression in high dose males and females. Halosulfuron did not produce an oncogenic response. The NOEL was 2500 ppm (108.3 mg/kg/d) in males and 1000 ppm (56.3 mg/kg/d) in females.

6.3 1-Year Oral Toxicity Study in Dogs Hazleton Labs America, Inc., Virginia Study no. HL-89-343 Report Date 7 Aug. 1991 (GLP)

Halosulfuron (98.7%) was administered orally in gelatine capsules to beagle dogs (6/sex/gp) at doses of 0, 0.25, 1.0, 10 and 40 mg/kg/day for 12 months. Dose levels were selected based upon

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the results of a 3-month capsule study in dogs. Complete gross and microscopic post-mortem examinations were performed on all animals. A limited number of organs were weighed.

One HD male died during week 50. There were no clinical observations prior to death, nor any noteworthy gross or histopathological findings. There were no clinical signs observed in other animals which were considered related to treatment. Body weight gain was decreased in males at 10 and 40 mg/kg by 21 and 23%, respectively, during the first 16 weeks of treatment, but subsequently, body weight gain in these groups was similar to controls. There were no treatment-related effects observed at ophthalmoscopic examination.

Mean erythrocyte, haematocrit and haemoglobin levels were slightly decreased in HD females, lymphocytes were moderately depressed in HD males, and cholesterol levels were slightly to moderately decreased in males at 10 and 40 mg/kg. Urinalysis parameters were not significantly affected. No noteworthy effects were observed on gross pathology, organ weights or histopathology; the incidence of pituitary cysts (0, 1, 0, 1, 2), while possibly increased at the HD (33.3%) was close to the historical control value of 28.9% (121 control females).

In conclusion, body weight gains, cholesterol levels and lymphocyte values were decreased in males and red cell parameters were decreased in females at 40 mg/kg. At 10 mg/kg, body weight gains and cholesterol levels were decreased in males. The NOEL was considered to be 1 mg/kg/day for males and 10 mg/kg/day for females.

7. REPRODUCTION STUDIES

7.1 Dietary Dose-Range-Finding One-Generation Study in Rats Inveresk Research International Limited, Scotland. Study no. IN-89-312. Report Date Feb. 1989, Study Completion Date 27 May 1988 (GLP)

Charles River CD Sprague Dawley rats (10/sex/gp) were fed halosulfuron (98.5%) at dietary levels of 0, 100, 400, 1600 and 6400 ppm. Treatment was for 4 weeks prior to mating, throughout mating, gestation and lactation. Seven days (? 9 according to data Tables) were allowed for mating (1:1 pairings). The day of detection of sperm and/or a copulatory plug in situ was designated Day 0 of gestation. The females were allowed to litter normally. The day on which parturition commenced was designated Day 0 of lactation. Litters were not culled. All animals (F0 and F1) were sacrificed on lactation day 21. F0 animals received a gross necropsy. F1 animals were examined externally.

Comment: The study summary incorrectly stated that dams and pups were necropsied on day 14 of lactation.

Achieved doses (calculated pre-mating only) ranged from 0, 8-12.9, 32.6-50.6, 129-199 and 549-815 mg/kg/d (lower intakes in males, higher in females).

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No clinical signs were reported. At 6400 ppm, male body weight gain was decreased 17.5% at week 4 and 18% by study termination at week 11. Female body weight gain in the 6400 ppm group was decreased 33% at week 4, 11% during the period of gestation and 18% during the lactation period. Female body weight gain was marginally reduced 6% at 1600 ppm during gestation but not during any other time period. Body weight gain in other treatment groups was similar to control. Food consumption in HD animals was slightly reduced over the first 1-2 weeks.

The mean number of implantations was slightly reduced at 6400 ppm only. There were no treatment-related effects on mating performance, length of gestation or on the birth index (number of pups born/number of implantation sites). The viability index (days 0-4 of lactation) was lower than control at 1600 ppm, marginally so at 6400 ppm; since this was not dose-related and viability in controls was lower than normal, it was not possible to determine if this effect was treatment related. Mean pup weights were lower than controls at birth and throughout lactation in the 1600 and 6400 ppm groups. The difference from control pup weights remained at approximately 12% during the lactation period at 1600 ppm, but steadily increased in the 6400 ppm groups from 12% at day 0 to 25% at day 21. Mean litter weights were also decreased at 6400 ppm from days 7-21 and at 1600 ppm for days 4-21.

In conclusion, maternal and paternal toxicity was indicated at 6400 ppm by reduced weight gain throughout the treatment period. Weight gain was marginally reduced in females at 1600 ppm during gestation. The mean number of implantations was slightly reduced at 6400 ppm. Decreased litter and pup weights were observed at 1600 and 6400 ppm. The NOEL for parental F0 animals was 1600 ppm (about 150 mg/kg/d for males, 185 mg/kg/d for females) and for F1 offspring was 400 ppm (38 mg/kg/d for F0 males, 47 mg/kg/d for F0 females).

7.2 Two-generation Dietary Reproduction Study in Rats. Hazleton Washington, Inc. Study no. HL-89-342. Report Date 24 Oct 1991. Study Completion Date: 29 Nov. 1990.

Sprague-Dawley rats (26/ sex/ group) were fed diets containing halosulfuron (98.7%) at target concentrations of 0, 100, 800 and 3600 ppm. After 14 weeks, F0 animals were mated to produce an F1 generation. Litters were culled to 8 pups on lactation day 4 and weaned on lactation day 21. 26 F1 rats/sex/gp were randomly selected to continue on the study as parental F1 animals. Following 14 weeks of treatment post weaning, F1 animals were mated to produce an F2a generation, and then, following a rest period, mated again to produce an F2b generation. All animals were maintained on test diets throughout the pre-mating, mating, gestation and lactation phases until sacrifice.

All F0 and Fl adults underwent gross necropsy. Selected tissues from all HD and control animals, and target tissues and gross lesions from LD and MD animals were examined microscopically.

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All culled pups found dead during the postnatal period, F1 weanlings not selected for mating, and all F2a and F2b pups underwent gross necropsy.

Mean F0 male compound intakes during the pre-mating period were 0, 7.4, 61.0 and 274.2 mg/kg/d, and for F0 females, 8.9, 69.7 and 319.9 mg/kg/d, with some variations in female intake during gestation and lactation.

There were no deaths or clinical signs in adult animals considered to be related to treatment. Body weight gains during the pre-mating period for F0 HD animals were reduced 7% in males and 19% in females. Bodywt gains were only slightly reduced in F1 HD adult animals during the pre-mating period. Parental weight gain was unaffected at the LD and MD. Food consumption was slightly decreased in F0 HD females and in F1 HD animals.

Mating, pregnancy and fertility indices were not affected by the compound. The numbers of litters produced were sometimes less than the required 20/group, but this was not treatment related.

Litter size and postnatal survival were unaffected by treatment, apart from a possible marginally decreased viability of HD F1 pups (live at day 4/liveborn = 99%, 97%, 94% and 91%. F1 pup weights were unaffected by treatment at day 0 of lactation (birth). At day 7 of lactation, F1 pup weights were less than control at the MD and HD. By day 21, pup weight differences were statistically Significant, being approximately 12 and 17% below controls at the MD and HD, respectively. MD and HD pup weights were within historical control range, and the control and LD pup weights actually exceeded the historical control range. Day 0 F2a pup weights were unaffected by treatment. F2a HD pup weights were reduced 8-9% at 21 (but within historical control range). F2b HD pup weights were reduced approximately 7% at day 0 of lactation (but within historical control range). No effect on HD pup weights was observed at other F2b weighing intervals.

Although always within historical control range, the decrease in pup weights at the high dose was consistent between generations and litters, and is considered related to treatment. Slightly lower pup weights observed in F1 LD and MD animals were considered random and not related to treatment due to the lack of an effect in the subsequent F2 generation (F2a and F2b litters), and because these values were well within or above historical control range.

There were no gross or microscopic pathology changes in parents or offspring which were related to treatment. In conclusion, halosulfuron was administered to Sprague-Dawley rats at dietary levels of 0, 100, 800 and 3600 ppm for two generations. Reduced parental body weight gain and reduced pup weights occurred at 3600 ppm. There were no treatment related effects on reproductive or fertility parameters. The NOEL was 800 ppm (61 mg/kg/d for F0 males, 69.7 mg/kg/d for F0 females).

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8. DEVELOPMENTAL STUDIES

8.1 Oral Dose-Range-Finding Teratology Study in Rats Hazleton Labs America, Inc., Virginia. Study no. HL-89-318. Report Date 24 Jan. 1989 Study Completion Date 18 Mar. 1988 (GLP)

In a preliminary dose-selection study, halosulfuron (98.5% in 0.5% CMC, 0.1% Tween 80) was administered by gavage at 0, 15, 50, 150 and 300 mg/kg/day to pregnant Charles River CD(SD)BR rats (6/gp) during gestation days 6 to 15. Dams were necropsied on day 20. Half of all foetuses were processed for visceral examination while the rest underwent skeletal examination.

All dams survived until scheduled sacrifice. There were no treatment-related clinical observations. Mean body weight and body weight gain were unaffected. Pregnancy rate was 100% in all groups. At all doses, mean foetal weights, foetal sex ratios and the mean numbers of viable foetuses, implantation sites and corpora lutea were comparable to the control group. There were no significant treatment-related effects on external, visceral and skeletal variations and malformations at any dose level; anophthalmia was seen in 1/45 15 mg/kg and 1/49 300 mg/kg fetuses, while 6/49 300 mg/kg fetuses had dilated ureter.

In conclusion, the NOEL for both maternal and developmental toxicity was the highest dose tested viz. 300 mg/kg/day (discounting the 12% incidence of dilated ureter, the only statistically-significant finding which might have had biological significance). Recommended doses for the main study were 75, 250 and 750 mg/kg.

8.2 Rat Oral Teratology Study Hazleton Labs America, Inc., Virginia. Study no. HL-89-321. Report Date 18 Dec. 1990 Study Completion Date 12 Jun. 1988 (GLP)

Halosulfuron (98.5% in 0.5% CMC, 0.1% Tween 80) was administered by gavage at 0, 75, 250 and 750 mg/kg/day to pregnant Charles River CD(SD)BR rats (25/gp) during gestation days 6 through 15. Dose levels were selected on results from pilot study no. HL-89-318. Dams were necropsied on gestation day 20. Half the foetuses from each litter were processed for visceral examination while the remainder underwent skeletal examination.

There were no deaths. Maternal weight gains at 750 mg/kg/day were reduced by 15% during the treatment period. Mean corrected body weight gains (minus uterine weights) for the 750 mg/kg animals were also reduced by 15%. Alopecia and urine staining were noted in several animals at 750 mg/kg. No body weight effects or clinical signs were observed at lower doses. Mean post-implantation loss was increased at 750 mg/kg/day (2.1 vs. 1.0 in control). Foetal body weights were decreased at 750 mg/kg by 24% in males and 22% in females compared to control weights. No effects on post-implantation loss or foetal body weights were observed at dose levels below 750 mg/kg. There were no treatment-related effects on number of viable foetuses and sex ratios.

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The total numbers of foetuses and litters with malformations were increased at 750 mg/kg (3.1% and 27%, respectively) compared to control (0.6% and 8%, respectively). External malformations observed only at the HD included malrotated hind limbs, filamentous tail and rudimentary tail. Soft tissue malformations observed only at 750 mg/kg included spinal cord agenesis, heart and/or great vessel malformation, adrenal agenesis and ectopic kidneys. Several skeletal malformations were noted in the 750 mg/kg group only; fused ribs, filamentous tail, rudimentary tail and vertebral anomaly with associated rib anomaly. One visceral variation (dilation of the lateral ventricles of the brain) and several skeletal variations were increased in HD foetuses. The incidences of variations at the MD and LD levels were comparable to controls. With respect to the anophthalmia and ureter dilation seen in the range-finding study, only 2/165 control fetuses had microphthalmia and 4/170 LD fetuses had dilated ureter.

Based on these results, the NOEL for both maternal and development toxicity was 250 mg/kg/day.

8.3 Oral Dose-Range-Finding Rabbit Teratology Study Hazleton Labs America, Inc., Virginia. Study no. HL-89-313. Report Date 12 Aug. 1988 Study Completion Date 23 Dec. 1987 (GLP)

Halosulfuron (98.5%, in 0.5% CMC and 0.1% Tween 80) was administered by gavage at 0, 75, 250, 750 and 1000 mg/kg/day to artificially inseminated Hazleton HRA :(NZW)SPF rabbits (6/gp) during gestation days 7 to 19. Dams were sacrificed on gestation day 29. Following external examination, each live foetus underwent visceral examination. The foetuses were then eviscerated and processed for skeletal examination.

Three animals at 1000 mg/kg/day and 2 at 750 mg/kg/day died or were sacrificed moribund. One animal at 1000 mg/kg/day, 1 at 750 mg/kg/day and 2 at 250 mg/kg/day aborted. One 75 mg/kg female delivered early on gestation day 29. Reduced activity was observed at the HD. Anorexia and a thin appearance were observed in animals between 250 mg/kg and 1000 mg/kg. Body weight gains during the treatment period (days 7-20) were severely reduced at doses of 250 mg/kg and above. The 75 mg/kg animals were slightly below controls in body weight gain. There were no viable foetuses at doses of 1000 and 750 mg/kg due to total litter resorptions. Nonviable foetuses were also observed at 250 mg/kg but not at 75 mg/kg or in the control group. Foetal body weights were slightly decreased at both 75 and 250 mg/kg. There were no treatment-related increases in external, visceral or skeletal variations or malformations. Based on these results, the maternal and foetal NOELs would be less than the lowest dose tested of 75 mg/kg/day. Recommended dose levels for a full study were 15, 50 and 150 mg/kg/d.

8.4 Rabbit Oral Teratology Study. Hazleton Labs America, Inc., Virginia. Study no. HL-89-322. Report Date 18 Dec. 1990 Study Completion Date 23 April1988 (GLP)

Halosulfuron (98.5%, in 0.5% CMC and 0.1% Tween 80) was administered by gavage at doses of 0, 15, 50 and 150 mg/kg/day to

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mated female Hazleton HRA:(NZW)SPF rabbits (17/gp) during gestation days 7 to 19. Dams were sacrificed on gestation day 29. Following external examination, each live foetus was sacrificed for visceral examination. All foetuses were then eviscerated and processed for skeletal examination.

One control and one 15 mg/kg doe were found dead on gestation day 8; these deaths were attributed to dosing procedure. Two LD and two HD females aborted. Due to the lack of a dose response and because abortions sometimes occur in one or two animals in controls, it is not possible to ascribe this to treatment. There were no treatment-related clinical observations. A substantially lower mean body weight gain during the treatment period (days 7-20) was observed in the 150 mg/kg group. Body weight effects were not observed at lower doses. There were no treatment related gross necropsy findings.

Mean total resorptions were increased at 150 mg/kg (2.6% vs 1.0% in control animals). There were no effects on this parameter at other doses. There were no treatment-related effects on foetal weight, foetal viability or sex ratios. There were no increases in external or visceral variations or malformations or in skeletal variations. There was an apparent increase in the skeletal malformation, forked/fused ribs, at the HD. However, if both a rib and a vertebral anomaly were observed in the same animal, this was recorded as a vertebral anomaly. No increase in the incidence of rib anomalies was apparent if rib and vertebral (with rib anomaly) results were combined. Based on these results, the NOEL for both maternal and developmental toxicity was 50 mg/kg/day.

9. GENOTOXICITY STUDIES

9.1 Gene Mutation

9.1.1 'Salmonella typhimurium' (Histidine Reversion) Test.

Hazleton Labs America, Inc., Maryland. Study no. HL-89-330. Report Date, 4 Mar. 1991 (GLP)

A preliminary toxicity screen was conducted with 'S. typhimuriurn' strain TA 100 at concentrations up to 10000 µg/plate of halosulfuron (98.5% pure). Based on these results, halosulfuron (1.0 to 10000 µg/plate) was tested in duplicate plate incorporation assays in strains TA 98, TA 100, TA 1535, TA 1537 and TA 1538 in the presence and absence of Aroclor-induced rat liver S9.

In the preliminary study, halosulfuron was toxic at 4999 µg/plate and above. In the definitive assays, toxicity was evident at 5000 µg/plate and above. No mutagenic activity was observed for halosulfuron with any of the tester strains. Concurrent positive and negative control appropriate for each strain gave the expected results.

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9.1.2 Chinese Hamster Ovary Cells in Culture: HGPRT Locus Mutation. Monsanto Co. Environmental Health Lab., St Louis. Study no. ML-90-127. Report Date 23 Jan. 1991 (GLP).

Halosulfuron was tested for mutagenic activity at the hypoxanthine-guanine phosphoribosyl transferase (HGPRT) locus with an 'in vitro' culture of Chinese hamster ovary (CHO) cells. Normal CHO cells are sensitive to the toxic effects of 6-thioguanine (6-TG) while mutated cells are resistant. Therefore, in the presence of 6-TG, mutated cells will form colonies while non mutated cells will die.

The toxicity of halosulfuron (98.2% pure) to CHO cells in the absence and presence of Aroclor-induced rat liver microsomal fractions was determined in preliminary range-finding studies. Preliminary mutation assays were then conducted to determine the optimal S9 concentration and an initial estimation of mutagenic potential. Final mutation assays were conducted to assess any concentration response relationship.

No significant cytotoxicity was observed in the range-finding study, but halosulfuron was insoluble at concentrations above 500 μg/mL. The preliminary mutation assays were conducted at halosulfuron concentrations ranging from 200 to 1000 μg/mL, with and without S9 concentrations of 1, 2, 5 and 10%. No treatment-related mutagenic responses occurred. The confirmatory assay was conducted at concentrations ranging from 100-1000 μg/mL, with and without 5% S9. No treatment-related mutagenic responses were noted at any level.

9.2 Chromosomal Effects Assays

9.2.1 Micronucleus Test 'in vivo' Mouse Study. Hazleton Laboratories America, Inc., Maryland. Study No. ML-89-331. Report Date 15 Jan. 1990 (GLP).

Halosulfuron was evaluated for its ability to induce micronuclei in bone marrow polychromatic erythrocytes of ICR mice.

Halosulfuron (purity 98.5%) was administered via gavage to ICR mice (15/sex/gp) at dose levels of 500, 1667 and 5000 mg/kg. Dose levels were chosen based on the results of an LD50 study in mice (HL-89-334) performed at the same laboratory. 5/sex/dose were killed at 24, 48 and 72 hours. Slides of tibial bone marrow preparations were scored for micronuclei and the polychromatic (PCE) to normochromatic (NCE) cell ratio. One thousand PCEs were scored per animal. The solvent, carboxymethylcellulose, was used as a negative control, and cyclophosphamide (CP) was used as a positive control.

No signs of cytotoxicity were observed at any of the dose levels tested. Halosulfuron did not induce significant increases in micronucleated PCEs at any of the sacrifice times. The positive control gave the expected results.

9.2.2 Mammalian Cytogenetics: Chinese Hamster Ovary Cells in Culture. Hazleton Labs America, Inc., Maryland. Study no. HL-89-333. Report Date 16 Aug. 1988 (GLP).

The ability of halosulfuron to induce chromosomal aberrations in vitro using Chinese hamster ovary (CHO) cells with and without metabolic activation was investigated.

In a preliminary cytotoxicity study, CHO cells were incubated with and without rat liver microsomes at concentrations from 18 to 1800 µg/mL of halosulfuron. In the absence of activation, the cells were incubated with both halosulfuron and bromodeoxyuridine (BrdU) for 25 hours. In the presence of activation, the cells were incubated with compound for 2 hours, washed and then incubated with BrdU for 23 hours. The shorter incubation period with microsomal activation was used to minimise the cytotoxic effect of the microsomal activation system. The cells were arrested at metaphase by incubating with colcemid for 2.5 hours, harvested, fixed, placed onto microscope slides, stained and examined. A total of 100 cells were examined from each concentration. to determine whether the cells were in the first (M1) or second (M2) cell cycle.

Cytotoxicity was evident at the top dose of 1800 µg/mL in the range finding assay without S9 and at doses of 180 µg/mL and above with S9. A dose-related cell cycle delay was observed at

180 µg/mL and above in the assay without activation, but no cell cycle delay was observed at any dose in the presence of S9. There was no significant increase in chromosomal aberrations at any of the doses, either with and without metabolic activation. Substantial chromosomal damage was noted in the positive controls.

9.3 Other Genotoxic Effects

9.3.1 Unscheduled DNA Synthesis in Mammals: Rat Primary Hepatocytes. Hazleton Labs America Inc., Maryland. Study no. HL-89-332. Report Date 3 May 1993 (GLP).

Freshly prepared rat primary hepatocytes were exposed to halosulfuron in the present of tritiated thymidine. In assay 1, fifteen concentrations from 1000 µg/mL to 0.025 µg/mL were initiated. Treatment at 1000 µg/mL was moderately toxic (71.5% to 119.4% survival). In assay 2, toxicity was different from that observed in assay 1 and, the experiment was terminated; after receipt of a new sample of halosulfuron, a third assay was initiated. In assay 3, twelve concentrations from 1010 µg/mL to 1.01 µg/mL were used. Cytotoxicity was similar to that observed in assay 2, and 6 concentrations were selected for analysis of nuclear labelling. Treatments from 253 µg/mL to 5.06 µg/mL covered good range of toxicity (79.3% to 100.9% survival) and were prepared for UDS analysis. None of the concentrations induced a significant increase in UDS.

10. OTHER STUDIES

Sulfonylurea Herbicide	SUSDP Entry	NOEL (mg/kg/d)	ADI (mg/kg/d)	Rat PO LD50 (mg/kg)
Bensulfuron	Appendix B	2.5	0.02	>4,900
Chlorsulfuron	S5	5	0.05	>5,500
Metsulfuron	Appendix B	1	0.01	>5,000
Sulfometuron	S5	2.5	0.02	>5,000
Thifensulfuron	S5	1. 25	0.01	>5,000
Triasulfuron	Appendix B	0.5	0.005	>5,000

Sulfonylurea Herbicide	Skin Irritation	Eye Irritation	Skin Sensitis'n
Bensulfuron	none	severe	none
Chlorsulfuron	none	slight	-
Metsulfuron	none	slight	none
Sulfometuron	slight	light	none
Thifensulfuron	moderate	moderate	none
Triasulfuron	slight	none	none

None supplied

TES2-1789

APPENDIX I

Poisons Schedules, NOELS, ADIs and Acute Toxicities for a Number of Sulfonylurea Herbicides

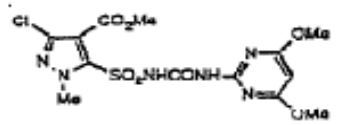
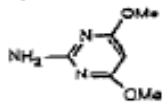
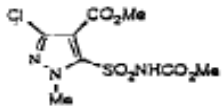
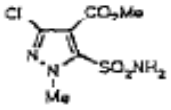
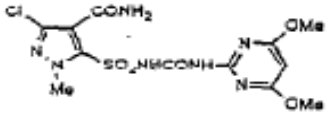
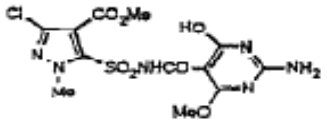
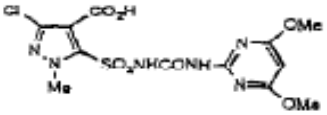
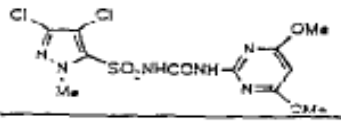
Available studies indicate that the above compounds were without carcinogenic, teratogenic or genotoxic potential (although oncogenicity and genotoxicity studies on file for chlorsulfuron were interim or incomplete).

TES2-I789

APPENDIX II

Structures of Impurities in Halosulfuron Technical

Name	Chemical name & Structure	CAS No

NC-319	Methyl 3-chloro-5-(4,6-dimethoxypyrimidin-2-ylcarbamoylsulfamoyl)-1-methylpyrazole-4-carboxylate	100784-20-1
		
ADMP	2-Amino-4,6-dimethoxypyrimidine	36315-01-2
		
CPSC	Methyl 3-chloro-5-methoxycarbonylsulfamoyl-1-methylpyrazole-4-carboxylate	135397-29-4
		
CPSA	Methyl 3-chloro-1-methyl-5-sulfamoylpyrazole-4-carboxylate	100784-27-8
		
319-AMIDE	3-Chloro-5-(4,6-dimethoxypyrimidin-2-ylcarbamoylsulfamoyl)-1-methylpyrazole-4-carboxamide	Not Available
		
319-SA	Methyl 5-(2-amino-4-hydroxy-6-methoxypyrimidin-5-ylcarbonylsulfamoyl)-3-chloro-1-methylpyrazole-4-carboxylate	Not Available
		
319-ACID	3-Chloro-5-(4,6-dimethoxypyrimidin-2-ylcarbamoylsulfamoyl)-1-methylpyrazole-4-carboxylic acid	135397-30-7
		
319-4CL	1-(3,4-Dichloro-1-methylpyrazole-5-sulfonyl)-3-(4,6-dimethoxypyrimidin-2-yl)urea	Not Available
		

ENVIRONMENTAL ASSESSMENT

Halosulfuron-methyl

In the Product

SEMPRA HERBICIDE BY MONSANTO

Prepared by

Chemical Section

Environment Protection Agency

PHYSICO-CHEMICAL PROPERTIES

Appearance:	Whitish odourless powder
Melting Point:	175.5-177.2oC
Relative Density:	1.62
Vapour Pressure:	< 1.4 x 10-8 kPa
Water Solubility:	The solubility in unbuffered distilled water is said in the Monsanto summaries of the aquatic toxicity tests to be about 36 mg.L-1. Solubility increases in buffered solutions, being 15 at pH 5, 1650 at pH 7 and 7470 mg.L-1 at pH 9 (at 20oC). Solubility declines with time at pH 9 due to instability.
Partition Coefficient:	
(n-Octanol/Water)	log P = 1.67 (pH 5), -0.02 (pH 7), -0.54 (pH 9). The substance is unstable in the aqueous layer at pH 9.
Dissociation Constant:	pKa 3.4. A1% slurry of the TGAC has a pH of 4.1.

FORMULATION OF END-USE PRODUCT

Sempra® is a dry flowable formulation containing 750 $g.kg^{-1}$ halosulfuron-methyl together with carriers and wetting and antifoaming agents, none of which appear to be new.

ENVIRONMENTAL EXPOSURE

Environmental Release

- Volume

In view of the restricted field of use, import volumes would not be expected to be large. The company has indicated that annual volumes of use at market maturity will remain below 10 tonnes.

- Application and use pattern

For control of the target weeds, Sempra® and a non-ionic surfactant will be diluted with water (at least 80 $L.ha^{-1}$) and applied by boom spray using flat fan nozzles at rates of65 to 130 g.ha-1 (50-100 g ai), depending on the intensity of infestation. This application method is expected to generate medium to large droplets with limited potential to drift. Spot treatments with handgun. Or knapsack sprayers will be used for areas of patchy infestation. The label recommends that weeds have a minimum of 5 cm new leaf growth for Nutgrass, and 2 cm for Mullumbimby couch.

93/4027

ENVIRONMENTAL ASSESSMENT REPORT

HALOSULFURON-METHYL

INTRODUCTION

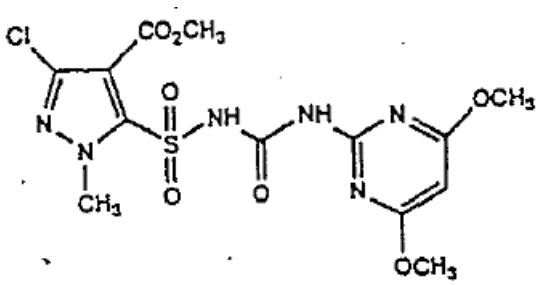
Monsanto Australia Limited has applied for clearance of a new technical grade active constituent, a sulphonylurea herbicide known as halosulfuron-methyl. Halosulfuron-methyl will be marketed in the product Sempra® Herbicide for post-emergence control of the perennial sedge species Nutgrass *(Cyperus ratundus)* and Mullumbimby couch *(Cyperus brevifolius)* in amenity turf situations, such as turf farms, golf courses, parks and ovals. .

Sempra® Herbicide is formulated in the USA as a dry flowable (water dispersible granule) from technical material manufactured by Nissan Chemical Industries. Ltd, Japan. Australian registration will be sought in NSW arid Queensland initially, but the applicant has indicated that trials are underway to extend this to other States. .

CHEMICAL IDENTITY

Name:	3-Chloro-5-[[[[(4,6-dimethoxy-2-pyrimidinyl)amino]carbonyl] amino sulphonyl]-1-methyl-1*H*-pyrazole-4-carboxylic acid, methyl ester.
Common name:	Halosulfuron-methyl
Other names:	NC-319 (TGAC), MON 12000, MON 12003, MON 12051, MON 12037, MON 12022.
CAS number:	100784-20-1
Molecular formula:	$C_{13}H_{15}N_6O_7SC1$
Molecular weight:	434.82

Structural formula:



Purity of TGAC: The Material Safety Data Sheet for NC-319 (dated 1 October 1992) specifies a purity of 97% minimum.

The sample provided had a purity of 99%.

Symptoms (gradual yellowing of foliage and seed heads, followed by dessication) appear within 7-10 d of spraying, with full effects reached after 4-6 weeks. The label indicates that follow up treatments may be applied where justified by new growth, up to a maximum seasonal rate of 260 g.ha^{-1}. Users are advised that spraying within 2 h of rain or irrigation will reduce control, and that mowing or cultivation should be delayed for at least 2 d following treatment. The target sedges are warm season weeds, and users are warned not to apply Sempra® after the onset of frosts or cool weather.

Turf areas where Sempra® may be used are located along the eastern seaboard of northern Australia. Current control options for the target sedges are limited. Short term control with combinations of bentazone, MCP A and dicamba is possible, or sequential high rate treatments of DSMA may be used for less sensitive turf species.

- **Formulation, handling and disposal**

Formulation will not expose the Australian environment to halosulfuron-methyl as it will be carried out overseas. Sempra® will be marketed in 1, 2, 2.5 and 5 L high density polyethylene containers.

Environmental Chemistry and Fate

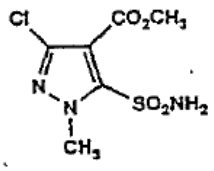
Studies submitted in this area may be summarized as follows:

A. Hydrolysis (reference 1)

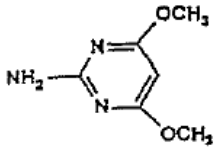
Buffered solutions (5 mg.L^{-1} at pH 5 and 7 or 9 mg.L^{-1} at pH 9) of halosulfuron-methyl, labelled in either ring, were incubated at 25°C for 30 d (46 h at pH 9) and analysed periodically by HPLC. The rate of hydrolysis increased with pH. Half-lives were 24.8 days, 14.9 days and 19.5

hours, respectively, for the pyrazole label, and 28.9 days, 13.9 days and 17.6 hours for the pyrimidine label.

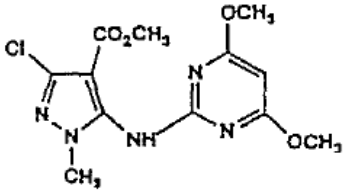
At pH 5, hydrolysis proceeds via cleavage of the sulphonylurea link to produce the aminopyrimidine and the pyrazolesulphonamide. At pH 9, hydrolysis of the sulphonylurea link is more rapid and accompanied by rearrangement. The pyrimidine and pyrazole rings become linked by an amino group in the alkaline hydrolysis product. At neutral pH, both mechanisms operate, the latter being approximately twice as fast. Some hydrolysis (in the order of 5%) of the carboxylic ester is also evident at neutral pH.



pyrazolesulphonamide (ester)



aminopyrimidine



amino-linked rearrangement product

The hydrolytic behaviour of halosulfuron-methyl differs from that of other sulphonylureas, which tend to be much more hydrolytic ally stable in their anionic forms (reference 2).

B. Photolysis

- **Aqueous (reference 3)**

Solution photolysis of halosulfuron-methyl, labelled in either ring, was investigated at pH 5 and 9, as hydrolytic degradation mechanisms differed with pH. Photolysis at neutral pH was not studied as both hydrolytic mechanisms operate at pH 7. Comparison of irradiated samples with dark controls indicated that the degradation observed was predominantly hydrolytic, with only minimal contributions from photolysis. Hydrolysis of the carboxylic ester approached 50% at pH 9 in this study, which was continued for 30 d.

- **Soil (reference 4)**

A non-sterile silt loam (pH 5) was fortified to a level of 35 $mg.kg^{-1}$ with halosulfuron-methyl (containing material radiolabelled in either ring as tracers) and exposed to natural sunlight for 30 d. Dark controls were incubated at 25°C, while daily mean temperatures to which the irradiated samples were exposed ranged between 13 and 27°C. Degradation involved cleavage of the sulphonylurea linkage and was more rapid in the dark controls, indicating that photochemical contributions were minimal.

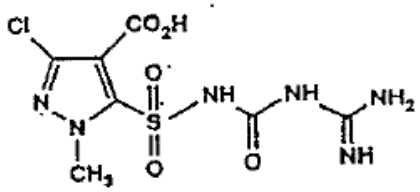
C. Degradation in Soil and Water

- **Aerobic soil metabolism (reference 5)**

Metabolism of halosulfuron-methyl was studied in two soils (see first two entries in table under adsorption/desorption) fortified to a level of 0.1 mg.kg-^{1} with radio labelled material and incubated at 25°C in the dark for a year.

Degradation in the acidic silty clay loam mainly involved cleavage of the sulphonylurea link to form aminopyrimidine and pyrazolesulphonamide metabolites, which are more persistent than the parent. The aminopyrimidine reached 26.7% of applied by the end of the experiment, while the pyrazole fragment peaked in its ester form at 29.3% after 2 months, and reached 32.1% in its acid form by study end. Halosulfuron acid peaked at 6.4% after 2 months.

An additional product (0.5% by study end) was identified as the guanidine derivative formed by .elimination of dimethyl malonate from the pyrimidine ring of halosulfuron acid. Evolution of $14C0_2$ amounted to 9.2% (pyrazole label) or 6.5% (pyrimidine label) of applied over



guanidine metabolite

the course of the study. The level of bound residues increased steadily to reach 33.7 or 54.6%, respectively.

Mineralisation was much more extensive in the alkaline sandy loam, with evolution of $14C0_2$ amounting to 33.2 or 62.3% of applied (pyrazole and pyrimidine labels, respectively) over the course of the study. The aminopyrimidine and pyrazolesulphonamide metabolites peaked at levels in the order of 5% in the first month of the ·study. As in the solution experiments, the amino linked rearranged product was also observed in the alkaline soil, peaking at 10.9% on the day of application. The guanidine derivative reached 14.9% after 6 months. The importance of ring cleavage in alkaline soil is underscored by the high rate of mineralisation of the pyrimidine ring. Halosulfuron acid peaked at 11.9% after 7 days. The level of bound residues increased steadily to reach 43.0% for pyrazole labelled material, and peaked at 27% after 112 days for pyrimidine labelled material before declining to 24.3% by study end.

A non-linear model was employed to calculate dissipation kinetics as the data obtained did not fit the traditional linear first-order model because of spatial variability in the dissipation process. The DT50, or first half-life, was 13.7 d (pyrazole label) or 18.3 d (pyrimidine label) in the acidic soil, while the DT90 was 103 or 116 d, respectively. Corresponding values in the alkaline soil were 13.6, 8.5, 69.4 and 57.1 d, respectively.

- **Anaerobic aquatic degradation (reference 6)**

This study was conducted to determine the rate and pattern of metabolism in oxygen-depleted water and hydrosoil. Duplicate experiments were conducted under nitrogen atmospheres for 12 months at a concentration of 0.10 $mg.L^{-1}$ in natural pond sediment and water (ratio 1:5) using material radiolabelled in either ring.

The nitrogen atmosphere was maintained for at least a month prior to introduction of the test substance, with glucose added two weeks before introduction to ensure viability of the anaerobic microorganisms. Original pHs of sediment and water were 7.0 and 7.9, respectively, but test media were markedly acidic (pH about 5) for the first 9 months of the study. Such low pH is typical of glucose amended anaerobic systems, and is thought to reflect the formation of acidic products from glucose metabolism.

As may be expected, the degradation involved cleavage of the sulphonylurea linkage. For pyrazole labelled material, the level of pyrazolesulphonamide increased steadily to reach about 90% of applied after 3-4 months, and remained at this 'level for the remainder of the study. The aminopyrimidine metabolite increased to about 80% of applied after 4 months in the pyrimidine labelled study, but declined to about 40% by study end. Mineralisation was not significant reaching 0.2% of applied in one of the pyrazole labelled samples, and not exceeding 1.4% for the pyrimidine labelled samples.

Assuming pseudo first-order kinetics, half-lives calculated for pyrazole and pyrimidine labelled halosulfuron-methyl were 27.2 and 18.8 days, respectively, in the same order as the hydrolytic half-life at pH 5. The amino and sulphonamide fragments persist under anaerobic conditions.

D. Mobility in Soils

- **Adsorption/desorption (reference 7)**

Batch adsorption/desorption experiments were conducted in duplicate on 1 g samples of four soils (see table) equilibrated for 6 hours with 5 mL buffered . solutions (four concentrations between 0.1 and 1 mg.L-^{1}) of radiolabelled halosulfuron-methyl, its aminopyrimidine metabolite, and the pyrazolesulphonamide fragment (ester and acid). Short equilibration times were used as separate experiments indicated that equilibrium was largely reached and the test substances were stable (< 5% degradation) within this timeframe. The alkaline sandy loam was equilibrated with a solution of the test substances in pH 7.7 buffer, while the remaining soils were treated with solutions in pH 5.5 buffer.

Soil Type	pH	oc	sand	silt	clay	CEC	Koc
Silty clay loam	5.8	2.0	7	62	31	30.3	178
Sandy loam	8.0	0.6	59	31	10	10.3	117
Silt loam	6.9	1.8	23	53	24	22.1	83
Loamy sand	6.8	1.2	77	19	4	6.3	28

Soil organic carbon partition coefficients tabulated above indicate that halosulfuron-methyl is typical of the sulphonylureas in that it sorbs rather weakly to soil, and has moderate to high mobility. The variability between soils indicates that other mechanisms besides sorption to organic matter have a significant influence on the mobility of halosulfuron-methyl, as may be expected for a weak acid. Note that the herbicide would have been almost completely ionised in solution as the pH of the most acidic soil was more than two units above the pKa.

The three metabolites are also hydrophilic compounds, with solubilities of 236000, 866 and 6490 mg.L^{-1} recorded at pH 7 for analytical samples of acid, ester and aminopyrimidine, respectively. Meaningful data could not be derived for the acid metabolite because of the very low degree of sorption (< 2%). However, it may be assumed that the acid is the most mobile of the four substances under investigation. The ester metabolite is more strongly bound than its parent, but still retains moderate to high mobility. Soil organic carbon sorption coefficients were 297, 138, 167 and 61, respectively. The aminopyrimidine metabolite was found to bind moderately to the silt loam, sandy loam and loamy sand (Koc 648, 331 and 225,respectively) and strongly to the silty clay loam (Koc 1612).

The Freundlich equation was also applied to data from two sequential desorptions. In general, the desorption coefficients exhibited an increasing trend relative to the initial sorption. No meaningful data were obtained for the highly mobile acid metabolite.

- **Leaching potential**

Field studies (see below) indicated that only small proportions (max 1.2% of applied) leached through 90 cm lysimeters. Much of this would have leached as metabolites, notably the hydrophilic acid form of the pyrazolesulphonamide metabolite.

The potential for pesticides to leach can be readily estimated from the nomogram of Gustafson (reference 8) provided that soil adsorption and persistence data from the field are available. Application of the soil organic carbon partition coefficients tabulated above and the field half-lives listed below generates a range of GUS values spanning the transition between probable and improbable leachers. Results indicate that leaching may occur in acidic sandy soils, particularly if soil temperatures are low. However, target sedges in Australia are warm season weeds, limiting this leaching potential. Laboratory half-lives return similar results, but without the outliers indicating probable leaching in cold soils.

E. Field Dissipation Studies

Halosulfuron-methyl was applied to sites in Texas and Illinois at a rate of 140 $g.ha^{-1}$, prior to the emergence of field corn (reference 9). The Texas soil was a clay loam with 1.2% organic carbon and a pH of 8.3 in the 30 cm surface layer. The Illinois soil was a loam with 2.8% organic carbon and a pH of 7.7 in the 15 cm surface layer, grading to a silty clay loam with 2.1% organic carbon and a pH of 8.0 in the underlying 15 cm layer. Half-lives calculated using a first order non-linear spatially variable model were 6 and 34 d, respectively.

As well as examining the dissipation of the parent, behaviour of its pyrazolesulphonamide (ester) and aminopyrimidine metabolites was investigated. Neither metabolite could be detected (limit 5 $\mu.1g.kg^{-1)}$ in any soil layer at any time during the 18 month studies. However, it should be remembered that cleavage of the sulphonylurea link is a minor degradation pathway at alkaline pH. The parent was only detected (limit 2 $\mu.1g.kg^{-1}$) in the surface layer in the Texas study, but reached 4 and 3 µ.1g.kg-1, respectively, in 15-30 and 30-45 cm layers 34 days after application in Illinois.

A second study (reference 10) utilised 90 cm in-ground soil columns and lysimeters at bare soil locations in North Carolina and Iowa. Soil at the North Carolina site was a sandy loam with 0.6% organic carbon and a pH of 6.0 at the surface, while that at the Iowa site was a loam with 1.3% organic carbon and a pH of 5.9 at the surface. Halosulfuron-methyl, radiolabelled in either ring, was applied at rates between 135 and 235 $g.ha^{-1}$. Sampling was to be continued for 18 months, but the interim report only contains data from the first 12 months.

Half-lives for dissipation of halosulfuron-methyl ranged between 4 and 10 days in North Carolina, and 14 and 56 days in Iowa. The slower dissipation at Iowa reflects seasonal factors as the trial was initiated late in the season. Less than 0.5%' and 1.2% of applied radiolabel leached through the lysimeters in North Carolina and Iowa, respectively.

F. Accumulation and bioaccumulation

Accumulation of halosulfuron-methyl in soils is not expected as it will be applied at most twice per season and has limited persistence. Metabolites are also not expected to accumulate as they too do not persist in soils.

Bioaccumulation tests were not conducted, but bioaccumulation would not be expected given the hydrophilicity and hydrolytic instability of halosulfuron-methyl.

G. Summary of Environmental Fate

Halosulfuron-methyl is a moderately to highly soluble and hydrolytically unstable sulphonylurea herbicide. Residues that are not taken up by turf are expected to become associated with interstitial water in the soil. However, the herbicide undergoes rapid degradation in soils to generate both hydrophilic metabolites and soil bound residues.

• Degradation rates and routes

Abiotic hydrolysis of halosulfuron-methyl proceeds rapidly, particularly at alkaline pH where it involves rearrangement of the sulphonylurea to an amino bridge, with a half-life less than a day. This behaviour is atypical of sulphonylureas, which tend to be hydrolytically stable as their conjugate bases. At acidic pH, the more usual cleavage of the sulphonylurea link to amino and sulphonamide metabolites proceeds with a half-life of about 3 weeks. Hydrolysis of the carboxylic ester may also be observed.

Similar pH dependent degradation is observed in soils. Both hydrolytic and microbial mechanisms would operate, the latter evident from the production of carbon dioxide from either ring, particularly at alkaline pH. Other routes for soil metabolism include elimination of dimethyl malonate to form a guanidine derivative. ..

• Metabolites

Primary metabolites at lower pH are the pyrazolesulphonamide ester and the aminopyrimidine. These metabolites are somewhat more persistent than the parent in aerobic soils, and markedly so under anaerobic conditions. At higher pH the initial metabolite is the amino-linked analogue which does not persist. Other metabolites include carboxylic acids (from ester hydrolysis) and a guanidine derivative formed by fragmentation of the pyrimidine ring. Extensive· mineralisation occurs, particularly in alkaline soils. Significant levels of bound residues are also formed, particularly in acidic soils.

- **Mobility**

Halosulfuron-methyl and its pyrazolesulphonamide metabolites sorb rather weakly to soils and are moderately to highly mobile, particularly the acid. The aminopyrimidine fragment sorbs moderately to strongly to soils.

- **Conclusion**

Halosulfuron-methyl is a hydrolytically unstable sulphonylurea herbicide that dissipates from soil principally through abiotic hydrolysis and microbial metabolism. It and its metabolites are not expected to accumulate in soils or biota because of their hydrophilicity and limited persistence. The latter property should exclude halosulfuron-methyl residues from groundwater.

ENVIRONMENTAL EFFECTS

The following tests were conducted according to US EPA Guidelines (reference 11).

A. Avian Toxicity

Test	Species	Result	Reference
Acute oral	Bobwhite quail	LD50 > 2250 mg.kg-1	12
5 d dietary	Bobwhite quail	NOEL> 5620 ppm	13
5 d dietary	Mallard duck	NOEL> 5620 ppm	14

The above results indicate halosulfuron-methyl to be practically nontoxic to birds, with neither lethal nor sub-lethal effects noted at any test concentration

B. Aquatic Toxicity

Test	Species	Result	Reference
96 h acute	Rainbow trout	NOEC = 26.7 ppm	15
96 h acute	Bluegill sunfish	NOEC = 21.4 ppm	16
48 h acute	*Daphnia magna*	NOEC=24ppm	17
120h growth	*Selenastrum*	EC50 = 5.3 ppb	18
inhibition	*capricornutum*	NOEC = 0.63 ppb	

120h growth	*Anabaena*	EC50 = 158 ppb	19
inhibition	*flas-aquae*	NOEC = 100 ppb	
120h growth	*Navicula*	EC50 > 350 ppb	20
inhibition	*pelliculasa*	NOEC = 350 ppb	
120h growth	*Skeletanema*	EC50 > 400 ppb	21
inhibition	castatum	NOEC = 400 ppb	
14 d frond	Lemna gibba G3	IC50 = 0.038 ppb	22
production		NOEC = 0.023 ppb	

Acute studies on rainbow trout used static renewal conditions with periodic measurement of dissolved concentrations by HPLC. These remained reasonably constant and close to nominal for concentrations near or below the solubility limit, said to be about 36 ppm in unbuffered distilled water. DMF was added to the test medium, and this together with the pH (ranging between 7.8 and 8.6) should have significantly enhanced the solubility. However, at the highest concentration tested (nominally 110 ppm) measured concentrations were extremely erratic, being on average about half of nominal. Precipitation of the test substance was said to be a visible consequence of addition of saturated DMF stock solutions to the medium-hard well water used for the study. The most extreme departures from nominal were recorded in freshly renewed systems, but appeared to return to nominal by the next renewal at concentrations near or below the solubility limit.

Another experimental anomaly is that the high pH of the test water should have catalysed hydrolysis of the test substance. This did not seem to occur as test concentrations did not decline significantly over 24 h intervals at concentrations near or below the solubility limit.

Rainbow trout appeared normal at all concentrations fested, except for one mortality after 72 hours at the highest concentration. However, a single mortality also occurred in controls. The no effect level was set at the highest verifiable test concentration, but is probably higher.

Similar anomalies characterised the bluegill and cladoceran studies and occurred even below the solubility limit, suggesting that preparation of the renewal water was inadequate. However, the results appear adequate to demonstrate that, like other sulphonylureas (reference 2) halosulfuron-methyl would be no more than slightly toxic to aquatic fauna.

Tests on aquatic flora used nominal concentrations as test concentrations were below the limit of quantitation. Analysis of test media containing 10 ppm of the toxicant indicated a slight reduction (typically about 20%) over the course of the tests. Test results confirm the high algal toxicity that would be expected of a sulphonylurea herbicide. The freshwater green alga. *Selenastrum capricornutum* and the duckweed *Lemna gibba* G3 are particularly sensitive, with the no effect levels for each being the lowest concentration tested. Apart from reduced frond production in duckweed, dead, chlorotic or necrotic fronds were noted as well as breakup of colonies and root destruction towards the end of the test at some intermediate concentrations. However, colonies appeared normal at the end of the test at the highest concentration tested (0.73 ppb) apart from the absence of new fronds.

C. Non-target Invertebrates

Halosulfuron-methyl is practically nontoxic to bees (LD50 > 100 µg.bee-1) exposed via the contact route (reference 23).

D. Mammals

Results of acute toxicity studies conducted on laboratory animals are from Part 1 summaries but give some indication of toxicity towards mammals in the absence of any wildlife data.

Test	Species	Result
Acute oral	Mouse	LD50 = 16156 mg. kg^{-1}(♂)
Acute oral	Mouse	LD50 = 9295 $mg.kg^{-1}$ (♀)
Acute oral	Rat	LD50 = 10435 $mg.kg^{-1}$(♂)
Acute oral	Rat	LD50 = 7758 $mg.kg^{-1}$ (♀
Acute dermal	Rat	LD50 > 2000 $mg.kg^{-1}$

The above results indicate that halosulfuron-methyl is practically nontoxic to· mammals.

E. Phytotoxicity

Halosulfuron-methyl has selective post-emergent activity against sedges and certain annual broad leafed weeds. Efficacy summaries indicate that phytotoxicity to a wide variety of ornamental annual and perennial woody and herbaceous plants varies from high to non-existent, depending on species, timing and application rate. The company concludes that some degree of phytotoxicity can be expected in Australia, and indicates on the label that spraying of non-target vegetation should be avoided.

F. Summary of Environmental Toxicity

Tests indicate halosulfuron-methyl to be practically non-toxic to birds, mammals,

aquatic fauna and bees. The ecotoxicological profile is typical for a sulphonylurea, with herbicidal activity the dominant feature. Halosulfuron-methyl is selective for sedges and certain annual broad leafed weeds. The herbicide is highly toxic to freshwater algae and duckweed.

PREDICTION OF ENVIRONMENTAL HAZARD

Halosulfuron-methyl will be largely intercepted by vegetation following application. Residues that are not so intercepted, or are washed off by rain or irrigation after application, will mainly become associated with interstitial water in the soil, where they are mobile but subject to rapid chemical and microbial degradation.

- **Terrestrial organisms**

As noted above, halosulfuron-methyl is practically non-toxic to birds and mammals. Terrestrial organisms will not undergo significant exposure to halosulfuron-methyl as it will be applied no more than twice a year at a relatively low rate.

- **Aquatic organisms**

As noted above, halosulfuron-methyl is practically non-toxic to aquatic fauna. If sprayed inadvertently over 15 cm of standing water at the maximum proposed rate, a concentration of about 70 $\mu g.L^{-1}$ would prevail, more than two orders 6f magnitude below no effect levels. Such levels would be likely to impact on freshwater algae and aquatic plants, however.

A more realistic exposure scenario via runoff may result in a concentration in the order of 5% of that arising from direct overspray, or about 3.5 ppb, indicating potential hazard to freshwater green algae and aquatic plants. Caution in the use of Sempra® is therefore warranted. The label warns against application if rain may follow within 2 hours. It should be noted, however, that such concentrations would not persist and that permanent damage to aquatic flora would not be expected from brief exposures of this magnitude. In addition, runoff from proposed use sites is likely to be mainly to artificial situations such as stormwater drains and retention ponds, rather than natural areas.

- **Desirable vegetation**

Hazard to non-target vegetation will be variable, but likely to be significant for some species if sprayed directly. The label warns against such practices.

CONTROLS/LABELLING

Halosulfuron-methyl must not be allowed to contaminate water, either accidentally or through normal use.

- **Formulation/Packaging**

As these operations are carried out overseas, no special controls are necessary.

- **Transport**

The small pack sizes will limit the potential for environmental contamination in the event of an accident.

- **Storage**

The draft label (see attached) is satisfactory.

- **Use**

The draft label is satisfactory.

- **•Disposal**

The draft label is satisfactory.

CONCLUSIONS AND RECOMMENDATIONS

Halosulfuron-methyl is a sulphonylurea herbicide that differs from its predecessors in hydrolysing rapidly at alkaline pH. Like other sulphonylureas, halosulfuron-methyl is moderately to highly mobile in soils. However, ready hydrolysis over the pH range normally encountered in the environment will minimise the risk that residues of halosulfuron-methyl will leach and enter groundwater. Even if such accessions did occur in vulnerable areas, hydrolytic instability would ensure their breakdown.

Halosulfuron-methyl has low toxicity to all fauna studied (birds, fish, cladocerans, bees and rodents) but high toxicity to some plants, notably the target sedges, certain broad leafed weeds, freshwater green algae and aquatic plants. Its mobility entails some risk to sensitive non-target vegetation, particularly aquatic. However, given limited persistence, the infrequency of application and warnings to avoid spraying, particularly of non-target vegetation and generally if rain may follow within two hours of application, significant damage to non-target terrestrial or aquatic flora is not expected.

Data submitted support the conclusion that use of Sempra® on turf according to label and good agricultural practice should not lead to significant environmental contamination or damage to non-target fauna and flora. In order to help validate this assessment, the company has agreed to alert the Environment Protection Agency immediately of any off-target incidents associated with the use of Sempra® that may arise.

REFERENCES

1. A Kesterson, B Lawrence and L J Lawrence, "Hydrolysis of ^{14}C-MON 12000 at pH 5, & and 9", Monsanto Report No MSL-11505 (PTRL Study No 454), November 1991.

2. E M Beyer, M J Duffy, J V Hay and D D Schleuter, "Sulphonylurea Herbicides", (Chapter 3 in "Herbicides: Chemistry, Degradation and Mode of Action, Volume 3", Marcel Dekker Inc, 1988).

3. A Kesterson and B Lawrence, "Solution Photolysis of ^{14}C-MON 12000 in Natural Sunlight", Monsanto Report No MSL-12097 (PTRL Study No 512), January 1993.

4. A Kesterson and B Lawrence, "Soil Surface Photolysis of [^{14}C]-MON 12000 in Natural Sunlight", Monsanto Report No MSL-12096 (PTRL Study No 561), July 1992.

5. K A Chott and M E Mehrsheikh, "Aerobic Soil Metabolism of MON 12000", Monsanto Report No MSL-10663, May 1991.

6. B Lawrence, S G Mobley, J Lambert and A Kesterson, "Anaerobic Aquatic Metabolism of [^{14}C] MON 12000", Monsanto Report No MSL 12568 (PTRL Study No 491), January 1993.

7. R G Nadeau and R S Sidhu, "Adsorption/Desorption Studies of MON 12000 and Three Aerobic Soil Metabolites", Monsanto Report No MSL 11288, October 1991.

8. D I Gustafson, "Groundwater Ubiquity Score: a Simple Method for Assessing Pesticide Leachability", *Environmental Toxicology and Chemistry*, 1989, 8, 339-357.

9. R K Beasley, "Dissipation of MON-12000 and MON 12000 Metabolites in Field Soil", Monsanto Report No MSL 12356, January 1993.

10. R H White and M A Schlicher, "Dissipation of RadiQlabelled MON-12000 and MON 12000 Metabolites in Field Soil", Monsanto Report No MSL 12463, January 1993.

11. EPA-540/9-82-024 "Pesticide Assessment Guidelines, Subdivision E, Hazard Evaluation: Wildlife and Aquatic Organisms" EPA, Washington DC, October 1982.

12. S Campbell, J Grimes and G J Smith, "MON 12000: An Acute Oral Toxicity Study with the Northern Bobwhite", Monsanto Study No WL-90-153 (Wildlife International Project No 139-268), March 1991.

13. J Foster, C P Driscoll, K A Hoxter and G J Smith, "MON 12000: A Dietary LC50 Study with the Northern Bobwhite", Monsanto Study No WL-90-154 (Wildlife International Project No 139-266), January 1991.

14. J Foster, C P Driscoll, K A Hoxter and G J Smith, "MON 12000: A Dietary LC50 Study with the Mallard", Monsanto Study No WL-90-155 (Wildlife International Project No 139-267), January 1991.

15. D Murphy and G J Smith, "MON 12000: A 96-Hour Static Renewal Acute Toxicity Test with the.Rainbow Trout (*Oncorhynchus mykiss*)", Monsanto Report No WL-90-549 (Wildlife International Project No 139A-117), November 1991.

16. D Murphy and G J Smith, "MON 12000: A 96-Hour Static Renewal Acute Toxicity Test with the Bluegill (*Lepomis macrochirus*)", Monsanto Report No WL-90-550 (Wildlife International Project No 139A-118), November 1991.

17. D Murphy and G J Smith, "MON 12000: A 48-Hour Static Renewal Acute Toxicity Test with the Cladoceran (*Daphnia magna*)", Monsanto Report No WL-90-551 (Wildlife International Project No 139A-119), November 1991.

18. S G Thompson and J P Swigert, "MON 12000: A 5-Day Toxicity Test with the Freshwater Alga (*Selenastrum capricornutum*), Monsanto Report No WL-92-178 (Wildlife International Project No 139A-151A), August 1993.

19. S G Thompson and J P Swigert, "MON 12000: A 5-Day Toxicity Test with the Freshwater Alga (*Anabaena flos-aquae*), Monsanto Report No WL-93-274 (Wildlife International Project No 139A-164A), June 1994.

20. S G Thompson and J P Swigert, "MON 12000: A 5-Day Toxicity Test with the Freshwater Diatom (*Navicula pellicllosa*), Monsanto Report No WL-93-275 (Wildlife International Project No 139A-163), June 1994.

21. S G Thompson and J P Swigert, "MON 12000: A 5-Day Toxicity Test with the Marine Diatom (*Skeletonema costatum*), Monsanto Report No WL-93-276 (Wildlife International Project No 139A-162), May 1994.

22. S G Thompson and J P Swigert, "MON 12000: A 14-Day Toxicity Test with Duckweed (*Lemna gibba* G3), Monsanto Report No WL-93-149 (Wildlife International Project No 139A-156), February 1994.

23. P A Winter, K A Hoxter and G J Smith, "MON 12000: An Acute Contact Toxicity Study with the Honey bee", Monsanto Study No WL-90-183 (Wildlife International Project No 139-265), December 1990

Box Label: Front Panel

DRAFT LABEL (8 August 1994)

WARNING

KEEP OUT OF REACH OF CHILDREN

READ SAFETY DIRECTIONS BEFORE OPENING

Sempra®

herbicide by Monsanto

ACTIVE CONSTITUENT: 750 g/kg HALOSULFURON-METHYL

For selective post-emergence control of Nutgrass and Mullumbimby couch in turf, as per directions for use.

READ THE ENCLOSED BOOKLET BEFORE USING THIS PRODUCT

Monsanto Australia Limited (A.C.N. 006 725 560)

600 St Kilda Road, Melbourne 3004

NET CONTENTS 100g or 600g

Sempra\100\600\0894\BOX1.2

Box Label: Front Panel

DRAFT LABEL (8 August 1994)

Sempra® herbicide by Monsanto

Safety Directions

Harmful if swallowed.

Dust will irritate the eyes.

Avoid contact with eyes and skin.

Wash hands after use.

First Aid

If poisoning occurs, contact a doctor or Poisons Information Centre.

Limit of Warranty and Liability

Monsanto Australia Limited ("Monsanto") warrants that this product conforms to the chemical description on the label. As the use of product sold is beyond· the control of Monsanto, no responsibility whatsoever for any consequences is accepted in respect of this product, save those non-excludable conditions implied by any State and Federal legislation or law of a Territory.

Not for re-packaging or re-formulation. No licence under any non-Australian patent is granted or implied by purchase of this product.

SPECIALIST ADVICE IN EMERGENCY: PHONE 008 033111

All Hours, Australia-wide

Refer to Monsanto Material Safety Data Sheet No. 238

Monsanto (logo)

Monsanto Australia Limited ACN 006 725 560

600 St Kilda Road Melbourne 3004

BAR CODE 9313771XXXX

Sempra\100\6oo\0894\80X2.2

Booklet

DRAFT LABEL (8 August 1994)

Sempra®

herbicide by Monsanto

DIRECTIONS FOR USE

For selective post-emergence control of Nutgrass and Mullumbimby couch in turf, as per directions for use.

For complete directions for use, read this booklet.

Sempra\100\600\0894IBK

Container label: Front Panel

DRAFT LABEL (8 August 1994)

WARNING

KEEP OUT OF REACH OF CHILDREN
READ SAFETY DIRECTIONS BEFORE OPENING

Sempra®

herbicide by Monsanto

ACTIVE CONSTITUENT: 750 g/kg HALOSULFURON-METHYL

For selective post-emergence control of Nutgrass and Mullumbimby couch in turf, as per directions for use.

READ THE ENCLOSED BOOKLET BEFORE USING THIS PRODUCT

Monsanto Australia Limited (A.C.N. 006 725 560)

600 St Kilda Road, Melbourne 3004

NET CONTENTS 100g or 600g

Sempra\100\600\0894\1.2.

Container Label: Back Panel

DRAFT LABEL (8 August 1994)

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All Hours, Australia-wide

Refer to Monsanto Material Safety Data Sheet No. 238

Monsanto (logo)

Monsanto Australia Limited ACN 006 725 560

600 St Kilda Road Melbourne 3004

Sempra\ 100\600\0894\2.2

GENERAL INSTRUCTIONS

Sempra herbicide can be used for selective control of Nutgrass *(Cyperus rotundus)* and Mullumbimby couch *(Cyperus brevifolius)* in turf as named in the **Directions for Use** table.

Symptoms of weed control are a gradual yellowing of foliage and. seed heads followed by desiccation. Initial symptoms may take 7-10 days to be noticeable, with full effects occurring 4 to 6 weeks after treatment.

Sempra should be applied to actively growing weeds when new growth has reached a minimum of 5 em of new leaf growth for Nutgrass or 2 cm for Mullumbimby couch. Apply follow-up treatments if sufficient new growth warrants after treatment.

Irrigation or rainfall within two hours of application will reduce control. Drought stress after treatment may also reduce control.

Mixing

Sempra is a dry flowable granule which disperses in water. Add the measured amount gradually to a part-filled spray tank while maintaining continuous bypass agitation. Add the surfactant near the end of the filling process to avoid excessive foaming. Remove the hose from the mixing tank immediately after filling to avoid siphoning back into the water source.

If allowed to stand, ensure that the mixture is thoroughly agitated before recommencing spraying. Use the mixture within one day.

Sprayer cleanup

Before application of products other than Sempra, the sprayer must be cleaned out as follows:

1. Drain the tank and flush equipment with water for a minimum of 10 minutes, including hoses, filters and boom.
2. Fill the tank with clean water and add chlorine bleach (containing 4% chlorine) at the rate of 300ml/100L of water. Flush through the boom and then agitate for 15 minutes. .
3. Repeat step 2 above.
4. Remove all nozzles and screens and clean thoroughly.
5. To remove traces of chlorine bleach, rinse the tank thoroughly with clean water and flush through hoses and boom.

Caution: Do not use chlorine bleach with ammonia. All traces of liquid fertilizer containing ammonia, ammonium nitrate or ammonium sulphate must be rinsed with water from the mixing

and application equipment before adding chlorine bleach solution. Failure to do so will release a gas with a musty chlorine odour which can cause eye, nose, throat and lung irritation. Do not clean equipment in an enclosed area.

Surfactant Addition

Sempra must be applied with a non-ionic surfactant to ensure uptake. Use 200mL/100L of a 600 g/L non-ionic surfactant or equivalent. For hand-gun or knapsack application, add surfactant at 20mL/10L of water.

Compatibility

Sempra is compatible with Hoegrass[1] dicamba/MCPA and bromoxynil/MCPA mixtures.

Protection of Crop, Native and Other Non-target Plants

Avoid spraying of non-target vegetation.

Do not use clippings from treated areas for mulching around vegetables or fruit trees.

Protection of Livestock, Wildlife, Fish, Crustacea, the Environment and others

Do not contaminate dams, rivers, or streams with the product or used container.

Do not feed grass clippings from treated areas to poultry or other livestock or allow grazing of treated turf.

Keep people and pets off treated areas until the spray solution has dried.

Storage and Disposal

Store in the closed, original container in a well-ventilated area, as cool as possible. Avoid prolonged storage in direct sunlight. Do not contaminate seed, food, feedstuffs or water by storage or disposal.

Triple rinse the empty container and add the rinsate to the spray tank or discard with the empty container. Dispose of the container and/or rinsate by burial under at least 500 mm of soil at an approved disposal site in a non-crop, non-pasture area away from water sources or homes. Empty containers should not be burnt and should be punctured, crushed or broken before disposal.

Safety Directions

Harmful if swallowed.

Dust will irritate the eyes.

Avoid contact with eyes and skin.

Wash hands after use.

First Aid

If poisoning occurs, contact a doctor or Poisons Information Centre.

Limit of Warranty and Liability

Monsanto Australia Limited ("Monsanto") warrants that this product conforms to the chemical description on the label. As the use of product sold is beyond the control of Monsanto, no responsibility whatsoever for any consequences is accepted in respect of this product, save those non-excludable conditions implied by any State and Federal legislation or law of a Territory.

Not for re-packaging or re-formulation. No licence under any non-Australian patent is granted or implied by purchase of this product.

SPECIALIST ADVICE IN EMERGENCY: PHONE 008 033 111

All Hours, Australia-wide

Refer to Monsanto Material Safety Data Sheet No. 238

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[1] Hoegrass is a registered trademark of Hoechst Schering AgrEvo.

Monsanto Australia Limited ACN 006 725 560

600 St Kilda Road Melbourne 3004

DIRECTIONS FOR USE (NSW and QLD ONLY)

RESTRAINTS

DO NOT use on turf greens

DO NOT apply more than 260 g/ha per season

DO NOT apply after the onset of frosts

DO NOT apply this product through any type of irrigation system

Situation	Weeds Controlled	Rate	Critical Comments
Established turf as named:· Buffalo grass *(Stenotaphrum . secundatum)* Carpet grass *(Axonopus affinis)* Durban grass *Dactyloctenium australa* Kikuyu grass *(Pennisetum c/andestinum* Couch *(Cynodon dactylon)* Couch. hybrid *(Cynodon*	Nutgrass *(Cyperus rotundus)* Mullumbimby couch *(Cyperus brevifolius)*	65·130 grams per hectare	Use higher rates on dense infestations. Apply to actively growing weeds when new leaf growth has reached a minimum of 5 cm on Nutgrass or 2 cm on Mullumbimby couch. Apply using a boom spray with flat fan nozzles 10 apply at least 80 L/ha of water. Apply follow-up treatments if sufficient new growth warrants re-treatment. For optimum control, mowing should be delayed for 2 days' following treatment. Use of this product on newly seeded. sodded or sprigged turfgrass that is not well established may result in damage and/or delayed establishment. In addition application to turf weakened by weather conditions or by physical damage due to intensive use or cultural practices such as scarification, coring, aeration or top-dressing, may result in damage and/or delayed recovery.

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

OCCUPATIONAL HEALTH AND SAFETY ASSESSMENT

HALOSULFURON-METHYL

In The Product

SEMPRA HERBICIDE BY MONSANTO

Prepared by

Chemical Assessment Branch

Worksafe Australia

OCCUPATIONAL HEALTH AND SAFETY ASSESSMENT

SEMPRA HERBICIDE

Halosulfuron-methyl

Monsanto Australia Limited

1. INTRODUCTION

Active constituent

Halosulfuron-methyl is not a hazardous substance. It was screened through the Health Effects Criteria, in the order given in the National Occupational Health and Safety Commission (NOHSC) Approved Criteria for Classifying Hazardous Substances (1).

Halosulfuron-methyl will at present be imported as formulated product, so no Australian workers will handle the active constituent alone.

According to Monsanto Australia Limited, halosulfuronmethyl is not classified as a dangerous good under the Australian Code for the Transport of Dangerous Goods by Road and Rail (ADG Code)(2). Therefore transport workers do not need to adhere to any special conditions when transporting it.

Halosulfuron-methyl has low acute toxicity by the oral, dermal and inhalational routes and is a slight eye irritant. The detailed discussion of toxicity occurs elsewhere in this Public Release Summary.

End Use Product

SEMPRA HERBICIDE is a hazardous substance. It was screened through the Health Effects Criteria, in the order given in the National Occupational Health and Safety Commission (NOHSC) Approved Criteria for Classifying Hazardous Substances (1), until it was determined to be hazardous on the basis of acute oral toxicity.

It is imported fully flowable waterdispersible granules, in small and big polyethylene plastic cans containing packed as dry up to 3kg (maximum) of product.

Hazardous substances are subject to the workplace controls outlined in the NOHSC Control of Hazardous Substances (3).

Future end use products containing halosulfuron-methyl should also be classified according to the NOHSC Approved Criteria for Classifying Hazardous Substances (I).

2. MANUFACTURE, FORMULATION, TRANSPORT, STORAGE AND SALE

This halosulfuron-methyl product has low toxicity by the oral, dermal and inhalational routes and is a slight skin and eye irritant.

Manufacture and formulation

Australian workers are not involved in the manufacture or formulation of halosulfuron-methyl or its product at this time.

Transport, storage and retail

As SEMPRA HERBICIDE will be imported final-packed into Australia, only transport, storage and retailing workers will handle it before end use. These workers could only become contaminated with the product under accidental conditions, for instance if the packaging were breached.

The product is not classified as a dangerous good under the ADG Code (2).

The risk of exposure to these workers is small and would involve low health and safety risks. The Safe Handling Information section in the Material Safety Data Sheet (MSDS) and the instructions on the label for the product provide sufficient information to enable workers to deal with spills.

Conclusion:

Sufficient control measures and instructions are available to enable the safe handling of SEMPRA HERBICIDE during transport, storage and retailing.

3. END USE including subsequent exposure to treated areas or animals

SEMPRA HERBICIDE will be applied by boom spray to control Nutgrass and Mullurnbimby couch in warm season turf. Monsanto Australia Limited suggests that the largest group of users will be amenity grass managers. Application rates per hectare for halosulfuron-methyl range between 48.8g to 97.5g, twice yearly. The concentration of halosulfuron-methyl in the applied spray ranges from 0.06% to 0.12%.

End users are most likely to be contaminated with the product via the skin. Acute toxicity of the product is such that end users are advised on the product label to avoid contact with eyes and skin. Worksafe Australia does not believe that any additional control by utilising personal protective equipment (PPE) is necessary, so PPE is not included on the label safety directions.

Based on the results of a long-term feeding experiment in dogs, Worksafe Australia does not believe that workers managing large or small areas of turf are at risk of suffering health effects from the long-term use of this product.

A restriction on entry into treated areas is not indicated at this stage, based on the low dermal and inhalational toxicity of SEMPRA HERBICIDE.

Conclusion:

The use pattern of SEMPRA HERBICIDE, coupled with its low toxicity and high dilution in working strength spray, enable it to be used safely with the control measures described above.

4. RECOMMENDATIONS

Transport workers, storage personnel and retail workers should use the Safe Handling Information in the MSDS and the label instructions for dealing with accidental exposure to halosulfuron-methyl products.

End users should follow the instructions, including the safety directions on the product label. They are instructed to avoid contact with eyes and skin. The label does not specify the use of PPE with SEMPRA HERBICIDE.

NOHSC has not established an exposure standard for halosulfuron-methyl and Worksafe Australia does not recommend that one be established at this time.

NOHSC has not placed halosulfuron-methyl on the Schedule for Health Surveillance (Schedule 3 Hazardous Substance for which Health Surveillance is Required) and Worksafe Australia does not recommend that NOHSC place it on the Schedule at this time.

WORKSAFE AUSTRALIA does not recommend a restricted entry statement for SEMPRA HERBICIDE at this time.

Manufacturers and/or importers of SEMPRA HERBICIDE should produce a MSDS for it and for other hazardous halosulfuron-methyl products in the future. Employers should obtain these from the supplier and ensure that all their employees have ready access to it.

Workers using SEMPRA HERBICIDE or any hazardous halosulfuron-methyl products in the future should read the MSDS.

5. REFERENCES

(I) National Occupational Health and Safety Commission, Approved Criteria for Classifying Hazardous Substances [NOHSC:1008(1994)], Australian Government Publishing Service, Canberra, 1994.

(2) Federal Office of Road Safety, Australian Code for the Transport of Dangerous Goods by Road and Rail, 5th Edition, Australian Government Publishing Service, Canberra, September, 1992.

(3) National Occupational Health and Safety Commission, Control of Workplace Hazardous Substances [NOHSC:1005(1994), 2007(1994)], Australian Government Publishing Service, Canberra, 1994.

Contd/ 2

6. MATERIAL SAFETY DATA SHEET

The MSDS for SEMPRA HERBICIDE is found in Attachment 1. It was provided by Monsanto Australia Limited as part of the submission for registration and is reproduced here as a matter of public record. The accuracy of this information remains the responsibility of Monsanto Australia Limited.

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Monsanto

Monsanto Australia Limited A.C.N. 006 725 560
600 St. Kilda Road. Melbourne. 3004
Telephone: 03 522 7122
EMERGENCY PHONE NUMBER 008 033111

MATERIAL SAFETY DATA

PRODUCT NAME

SEMPRA* Herbicide

IDENTIFICATION

MSDS No. 238 Date: 21/06/1994 Supersedes: 08/04/1994

Other Names:

MON 12037: MON 12022:

Dry flowable formulation containing HALOSULFURON-METHYL 750 g/kg

Use:

Herbicide. NOT FOR REFORMULATION OR REPACKING

Manufacturer's Name and Address

Monsanto Company

St Louis, Missouri

USA

U.N. Number:	N/A
Dangerous Goods:	N/A
Subsidiary Risk:	N/A
Packaging Group:	N/A
Hazchem Code:	N/A
Poisons Schedule:	5
EPG/GTEPG:	N/A

PHYSICAL DESCRIPTION/PROPERTIES

Appearance and Odour: Beige granules

Odour: Scorched vanilla

Boiling Point (C):	N/A	Specific Gravity:	N/A
Vapour Pressure:	N/A	Melting Point(C):	Not available
Vapour Density:	N/A	Evaporation Rate:	N/A
Solubility(Water):	Dispersible	Percent Volatiles:	None
Bulk Density:	0.6 kg/L	pH (1%solution):	6.6

FIRE/EXPLOSION HAZARD

Flash Point (C): This material is not combustible as tested by the Tag Closed Cup test.
Autoignition: Not applicable

LEL: Not applicable UEL: Not applicable

INGREDIENTS
Ingredient

HALOSULFURON-METHYL

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INGREDIENTS	CAS No:	Proportion:
Ingredient	100784-20-1	75.5 % w/w
HALOSULFURON-METHYL	1332-58-7	8-13 % w/w
KAOLIN	112926-00-8	<3 % w/w
SILICA, AMORPHOUS PRECIPITATED		Balance
CARRIER,BINDING AND ANTIFOAM AGENTS		

HEALTH HAZARDS

The following information summarizes human experience and the results of scientific investigations reviewed by health professionals for hazard evaluation of the material and the development of precautionary and safe handling procedures recommended in this document.

Effects of Exposure:

Dermal contact and inhalation are expected to be the primary route/s of occupational exposure to this material. Occupational exposure to this material has not been reported to cause significant adverse health effects. On the basis of available information, exposure to this material is not expected to produce any significant adverse human health effects when recommended safety 'precautions are followed.

Toxicological Data:

Data from Monsanto studies with this formulation in a powder form indicate the following:

Oral:	Slightly toxic	(LD50 rat 1287 mg/kg)	Cat. IV
Dermal:	Practically non-toxic	(LD50 rabbit>5000 mg/kg)	Cat. III
Eye Irritation:	Moderately irritating	(Rabbit FSHA)	Cat. III
Skin Irritation:	Slightly irritating	(Rabbit FSHA)	Cat. IV
Acute Inhalation:	Practically non-toxic	(Rat LC504-hr >5.7 mg/L)	Cat. IV
Dermal Sensitization:	Not a sensitizer	(Guinea pig)	

COMPONENTS

Data from Monsanto studies and from the scientific literature for the material indicate the following:

COMPONENT: Halosulfuron-methyl

Halosulfuron-methyl is considered to be practically non-toxic orally or by inhalation and no more than slightly toxic dermally. It is slightly irritating to eyes and essentially non-irritating to the skin. It did not produce skin allergy in guinea pigs.

Following repeated exposures (90-days) to halosulfuron-methyl in the feed, rats showed decreased weight gain, slight biochemical alterations, and effects on the kidneys and liver (NOEL 20 mg/kg). Dogs similarly treated showed decreased body weight gains. decreased cholesterol and effects on the kidney and blood (NOEL 10 mg/kg). Rats treated (21 days) with the material by skin application showed no adverse effects considered related to treatment (NOEL >1000 mg/kg). The material did not produce tumours in rats or mice following long-term (2-year) dietary exposures. Developmental toxicity, including re-sorptions, decreased pup weights and malformations, was observed in the presence of maternal toxicity in rats given halosulfuron-methyl orally during pregnancy (NOEL 2S0 mg/kg). Decreased maternal weight gain and an increase in post-implantation loss was seen in rabbits given the material during pregnanacy (NOEL SO mg/kg). Reduced parental and pup weights were noted in male and female rats given the material for two successive generations (NOEL 40 mg/kg); there were no adverse effects on reproduction or fertility. The material produced no genetic changes in a series of standard tests using animals or animal cells.

See Other Information for additional Toxicological Data on components.

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SWALLOWED

Harmful if swallowed.

SKIN

Slightly irritating to skin.

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EYE

Moderately irritating to eyes.

INHALED

May cause respiratory tract irritation.

FIRST AID

SWALLOWED

If swallowed. remove visible particles from mouth and rinse thoroughly with water. Swallow water to dilute. Seek medical advice.

NEVER GIVE ANYTHING BY MOUTH TO AN UNCONSCIOUS PERSON.

EYE

Hold eyes open, flood with water for at least 15 minutes and see a doctor.

SKIN

Remove contaminated clothing and wash skin thoroughly. Launder contaminated clothing before reuse.

INHALED

Remove to fresh air.

Get medical attention if breathing difficulty develops.

ADVICE TO DOCTOR

If further treatment guidance is required. contact Emergency Number.

PRECAUTIONS FOR USE

EXPOSURE STANDARDS

Airborne Exposure Limits:

PRODUCT: MONTURF Herbicide 100% w/w

ACGIH TLV/8-hr TWA: None Established.

COMPONENT: Silica. amorphous precipitated

Australian National Exposure Standard TWA: 10 mg/cubic metre

COMPONENT: Kaolin <1% crystalline silica)

Australian National Exposure Standard TWA: 10 mg/cubic metre

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ENGINEERING CONTROLS

Provide ventilation to control exposure levels below airborne exposure limits. Use local mechanical exhaust ventilation at sources of air contamination such as open process equipment.

PERSONAL PROTECTION

Precautionary Measures:

Avoid contact with eyes. skin and clothing. Avoid breathing dust. Wash thoroughly after handling.

Eye Protection:

Wear safety goggle when direct contact with excessive airborne dust is

likely.

Skin Protection:

Avoid contact as good industrial hygiene practice.

Wash hands and contaminated skin thoroughly after handling.

Respiratory Protection:

Avoid breathing dust. Use appropriate equipment when airborne exposure limits are exceeded. Consult respirator manufacturer to determine appropriate type of equipment for given application. The respirator use limitations specified by the manufacturer must be observed. Respiratory protection programs must be in compliance with AS 1715 and AS 1716.

Avoid breathing spray mist.

FLAMMABILITY

Not combustible or flammable.

See Safe Handling Information - Fire/Explosion Hazard.

SAFE HANDLING INFORMATION

STORAGE AND TRANSPORT

Store under cool, dry conditions. Do not store under moist conditions. The shelf life of this material is expected to be at least two years under normal conditions of storage (<35 C). Do not contaminate water, food, seed or feed by storage or disposal.

Australian Transport Code:

. Label: N/A Packaging Group: N/A EPG/GTEPG: N/A

SPILLS AND DISPOSAL

Spill or Leakage Procedures:

Observe all PRECAUTIONS FOR USE, including use of rubber boots or rubber overshoes, when cleaning up spills. Collect solid material and place in a metal or plastic-lined container and dispose of in accordance with instructions provided under Waste Disposal. After all material is removed, wash floors and other impervious surfaces with an industrial detergent solution and rinse with water.

Waste Disposal:

Wastes that cannot be used according to label instructions or chemically re-processed should be disposed of in a landfill approved for pesticide disposal. Dispose of in accordance with all applicable local and state laws. Avoid contamination of fertilizers, spray materials, seed, feed, foodstuffs or water by storage or disposal.

Containers:

Emptied containers retain material residue. Observe all labelled safeguards until container is cleaned, reconditioned or destroyed. Consult appropriate regulatory officials for information on disposal.

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FIRE/EXPLOSION HAZARD
Extinguishing Media:
Not combustible. Use appropriate extinguishing media for exposure fire.
Special Fire-fighting Procedures:
Fire fighters or others exposed to products of combustion from exposing fire should wear full protective clothing including self-contained breathing apparatus.
Thoroughly decontaminate equipment after use.
Unusual Fire and Explosion Hazards:

None

Reactivity Data:	
Stability	- shelf life expected to be at least two years under normal conditions of storage
Incompatibility	- none known
Hazardous decomposition products	- none known
Hazardous polymerization	- does not occur

SPECIAL NOTES
Warning Statements:
WARNING.
KEEP OUT OF REACH OF CHILDREN.
READ SAFETY DIRECTIONS ON LABEL BEFORE OPENING.
Harmful if swallowed.
Avoid contact with eyes and skin.
Do not inhale dust.
Wash hands after use.

OTHER INFORMATION
Toxicological Data on components (continued):
COMPONENT: Kaolin (containing <1% crystalline silica)

Inhalation of excessive amounts of kaolin dust may produce coughing, sneezing and nasal irritation. Long-term over-exposure to kaolin dust may cause respiratory difficulties, such as decreased lung capacity.

COMPONENT: Silica, hydrated amorphous
Inhalation of silica dust can cause drying of mucous membranes of the eyes, nose and throat (due to absorption of moisture and oils) which may result in irritation and occasional nose bleeds. Repeated exposure to silica gel has NOT been reported to have significant adverse health effects in workers. However, persons with breathing problems or lung disease may be at an increased risk. Laboratory studies in animals exposed by inhalation to silica gel have shown no adverse effects.

Environmental Effects of Halosulfuron-methyl:

96-hr LC50 Bluegill sunfish:	Slightly toxic	>21.4 mg/L
96-hr LC50 Rainbow trout:	Slightly toxic	>26.7 mg/L
4B-hr LC50 Daphnia magna:	Slightly toxic	>24.0 mg/L
5-day dietary LC50 Bobwhite quail:	Practically non-toxic	>5620 ppm

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5-day dietary LC50 Mallard duck:	Practically non-toxic	>5620 ppm
Acute oral LD50 Bobwhite quail:	Practically non-toxic	2250 mg/kg
Acute contact LD50 Honey bee:	Practically non-toxic	>100 microg./bee

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FOR ADDITIONAL NON-EMERGENCY INFORMATION. CALL:

MONSANTO AUSTRALIA LIMITED

ALL PRODUCTS:

Head Office: 600 St Kilda Road. Melbourne 3004 Phone (03) 522 7122

AGRICULTURAL PRODUCTS ONLY:

Queensland:	301 Coronation Drive. Milton 4064	Phone (07) 368 3088
New South Wales:	235 Lords Place. Orange 2800	Phone (063) 61 8200
West Australia:	18 Howe Street. Osborne Park 6017	Phone (09) 446 6500

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NOTE: The physical data are typical values based on material tested but may vary between samples. Values should not be construed as a guaranteed analysis of any specific lot or as specifications for the product.

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N/A* not applicable.