Public Release Summary
on

Evaluation of the new active

RIMSULFURON

in the product

DUPONT TITUS®HERBICIDE

National Registration Authority
for Agricultural and Veterinary Chemicals

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Canberra
Australia

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[redacted]

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FOREWORD

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

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

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

The information and technical data required by the NRA to assess the safety of new chemical products and the methods of assessment must be undertaken according to accepted scientific principles. Details are outlined in the NRA's publications *Ag Manual: The Requirements Manual for Agricultural Chemicals* and 7*Ag Requirements Series.*

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

More detailed technical assessment reports on all aspects of the evaluation of this chemical can be obtained by completing the order form in the back of this publication and submitting with payment to the NRA. Alternatively, the reports can be viewed at the NRA Library, Third floor, 10 National Circuit, Barton, ACT.

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

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LIST OF ABBREVIATIONS AND ACRONYMS

ac	active constituent
ADI	acceptable daily intake (for humans)
AHMAC	Australian Health Ministers Advisory Council
ai	active ingredient
d	Day
EC_{50}	concentration at which 50% of the test population are immobilised
EUP	end use product
Fo	original parent generation
h	Hour
HPLC	high pressure liquid chromatography *or* 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
LC_{50}	concentration that kills 50% of the test population of organisms
LD_{50}	dosage of chemical that kills 50% of the test population of organisms
mg	Milligram
mL	Millilitre
MRL	maximum residue limit
MSDS	Material Safety Data Sheet
NDPSC	National Drugs and Poisons Schedule Committee
ng	Nanogram
NHMRC	National Health and Medical Research Council
NOEC/NOEL	no observable effect concentration/level
po	Oral
ppb	parts per billion
PPE	Personal Protective Equipment
ppm	parts per million
s	Second
sc	Subcutaneous
SC	suspension concentrate
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

SUMMARY

The National Registration Authority for Agricultural and Veterinary Chemicals (NRA) has before it an application to register the product DuPont Titus® herbicide which contains the new active ingredient, rimsulfuron. The product's claims are the suppression of Blackberry Nightshade and control of certain broadleaf weeds in tomatoes (processing).

This publication outlines the regulatory considerations and provides a summary of the data evaluated for the proposed registration of DuPont Titus® herbicide. Before determining whether to register this product for use in Australia, the NRA invites public comment.

Comments should be submitted by **21 October 1998** to [redacted]

The NRA has assessed the data submitted by the applicant in support of the proposed use of rimsulfuron and provides the following information for public comment.

DuPont Titus® herbicide is formulated as a dry flowable water dispersible granule containing 250 g/kg of rimsulfuron. Currently there are very few options for tomato growers for the control of blackberry nightshade, *Solanum nigrum L.* Chipping is the only method of control. Due to blackberry nightshade being taxonomically very close to tomatoes, it is by far the most difficult and serious weed pest.

A herbicide such as Titus which is able to give significant suppression (and some mortality) of blackberry nightshade growth as well as mortality of other broadleaf weeds will be a welcome and vital alternative or additional management tool for tomato growers.

Public health aspects

Toxicology

A substantial package of toxicology data has been supplied in support of the application for approval of the new active ingredient, rimsulfuron, and the product DuPont Titus® herbicide, a solid (dry flowable water dispersible granules) with 25% active ingredient. Acute studies show that rimsulfuron has low toxicity for laboratory animals. Acute oral, dermal and inhalational toxicities were shown to be low for both the active ingredient and the end-use product. Neither rimsulfuron alone nor the product caused dermal irritation or acted as skin sensitisers but both have been classified as moderate eye irritants.

Repeat-dose studies in mice, rats and dogs have shown that the toxic effects of rimsulfuron relate mainly to decreased bodyweight gain and food consumption. Effects on haematology and clinical chemistry did not show a consistent pattern across all studies but in some instances were indicative of adaptation to an increased chemical load, as were increases observed in liver weights. The absence of microscopic changes in the liver, other than increased cell size, supported the conclusion of an adaptive response. A diuretic effect was a common finding at higher doses. Other organs were also affected in some studies (spleen, kidney, testes) and microscopic examination revealed increased age related changes in the testes in both the chronic mouse and dog studies at the highest doses used in those studies.

An increased incidence of cataracts was seen in female mice at 1500 mg/kg bw/day after 18 months and corneal opacities caused by lipid deposition, were seen in some dogs at 360 mg/kg bw/day.

Reproduction and developmental studies were unremarkable, the main effects being decreased bodyweight gain for adults before mating, females during gestation, and in offspring. A battery of genotoxicity studies showed no signs of mutagenicity, chromosome or DNA damage with rimsulfuron, and tumour incidences were unaffected in chronic studies.

Conclusion

Based on an assessment of the toxicology and the potential dietary intake of residues, it was considered that there should be no adverse effects on human health from the proposed use of rimsulfuron as a component of DuPont Titus® herbicide.

Residues in food and trade aspects

Residues in food

Results from Australian residue trials on tomatoes showed that rimsulfuron residues in the harvested tomatoes and in the tomato forage after a 4 weeks harvest withholding period were non-quantifiable (≤0.05 mg/kg).

When DuPont Titus® herbicide is used according to the proposed use pattern on tomatoes grown for processing, rimsulfuron residues in animal commodities as a result of animals having eaten produce made from the treated tomatoes or tomato forage and fodder are not expected to be quantifiable.

Trade

As the proposed use is expected to result in non-quantifiable residues, there appear to be no trade disadvantages from use on tomatoes. The presence of non-quantifiable residues of rimsulfuron in tomato crops also indicates that the use of tomato forage or fodder or processing waste, etc. as animal feed would not be expected to result in quantifiable residues in animal commodities.

Occupational health and safety aspects

The National Occupational Health and Safety Commission (NOHSC) has conducted a risk assessment on DuPont Titus® herbicide (Titus) containing rimsulfuron at 250 g/kg as dry flowable water dispersible granules for use on tomatoes. Titus can be safely used by workers when handled in accordance with the control measures indicated in this assessment.

Rimsulfuron is not listed as a hazardous substance in the NOHSC List of Designated Hazardous Substances. It is not determined to be a hazardous substance according to NOHSC Approved Criteria for Classifying Hazardous Substances. Titus cannot be determined to be a hazardous substance based on NOHSC criteria.

Titus will be imported fully formulated. It is packaged in 200 g jars. Transport, storage and retail workers will handle the packaged product; therefore, they could only become contaminated in the event of a packaging breach.

Titus has low acute oral, dermal, and inhalation toxicity. It is a moderate eye irritant, but has no skin irritant or skin sensitising properties.

The product is diluted with water, mixed with a non-ionic surfactant, and applied as a ground spray. The application rate is 60 g product/ha in a total spray volume of 50 L spray/ha. A second application can be made at the same rate 7 to 14 days later.

No worker exposure data was available for rimsulfuron or Titus. The occupational health and safety risk assessment was based on estimates obtained from exposure models.

Instructions and Safety Directions are provided on the product label to minimise exposure to the product. Mixer/loaders need to wear a face shield or goggles when handling the undiluted product. No Re-entry Period is recommended for Titus at this stage. Additional information is available on the product Material Safety Data Sheet (MSDS).

Environmental aspects

Application of rimsulfuron for weed control in tomato crops may result in contamination of the soil compartment within the treated area due to direct spray, spray drift or excess spray running off leaves, and off-site contamination could result from direct overspray, spray drift or run-off.

Environmental fate

Rimsulfuron hydrolyses in the dark and with exposure to sunlight at a fairly rapid to very rapid rate at 20-25°C, the rate of degradation being fastest at pH 9 and slowest at neutral pH ($t_{1/2}$ = 1.5-4.7 days, 7.1-24.7 days and 4.5-14.8 hours, at pH 5, 7 and 9, respectively). Hydrolysis also appears to be important in aerobic and anaerobic soil metabolism, where half lives determined depended on soil temperature and moisture content, ranging from 5 days at 60% maximum soil water holding capacity and 20°C to 77 days at 40% maximum soil water holding capacity and 5°C, and in aquatic metabolism studies, where half lives were 0.4-2.1 days at 25°C and 48-77 days at 5°C. Field dissipation half lives determined were 5.4-9.6 days in three sites under warm conditions and 15.9-17.7 days at a fourth, cooler site. A similar range of major metabolites were produced in most studies to those in the hydrolysis studies, the main degradation route being production of bridge contraction products, rather than cleavage of the molecule at the sulfonyl bridge, with sunlight and microbial activity leading to greater production of polar substances and in some cases, limited mineralisation of the labelled portions of the molecule.

Laboratory thin layer chromatography, soil adsorption/desorption and column leaching studies indicated that rimsulfuron has high to very high mobility in soil, but field dissipation studies showed little downward movement of the substance or its metabolites, moreover, the susceptibility of the molecule to hydrolysis is such that contamination of groundwater is not expected. Because it should degrade rapidly in water and soil, particularly under conditions pertaining in the short period each year when it may be used (spring/early summer in well-irrigated tomato crops), rimsulfuron is not expected to accumulate in soil or water, or to bioaccumulate in fish. The major degradation products IN-70941 and IN-70942 are more persistent, but the potential for their accumulation will be minimised by crop rotation preventing repeated annual application to the same area of soil.

Environmental effects

Rimsulfuron is practically non-toxic to birds, mammals, fish and aquatic and terrestrial invertebrates. It is moderately toxic (EC50 for biomass production at 72 hours = 1.2 mg ai/L nominal initial concentration) to the freshwater green alga, *Selenastrum capricornutum*, and may be highly to very highly toxic to the freshwater diatom, *Navicula pelliculosa*, (EC25 for cell count and biomass at 120 hours < 30 µg/L from a single rate test, but lower toxicity was indicated when a range of rates was tested with this species). Single concentration studies with rimsulfuron and the freshwater green alga, *Selenastrum capricornutum*, the freshwater blue-green alga, *Anabaena flos-aquae*, and the marine diatom *Skeletonema costatum* indicated NOECs ≥ 29 µg ai/L, 35 µg ai/L and 48 µg/L measured initial concentrations, respectively. However, rimsulfuron was found to be very highly toxic to the freshwater duckweed, *Lemna gibba* (MATC and EC50 for frond biomass dryweight = 0.97 and 11.6 µg/L, respectively; MATC for number of fronds produced = 0.09 µg/L, based on nominal initial concentrations adjusted for % recovery in the stock solution used to prepare test solutions). Phytotoxicity may also be expected to some species of non-target terrestrial plants. The major metabolites IN-70941 and IN-70942 both appear to have lower toxicity to various aquatic and terrestrial species than the parent substance.

Environmental hazard

The use of rimsulfuron as proposed in processing tomato crops is not expected to present a hazard to birds, mammals, terrestrial invertebrates and soil micro-organisms, nor to fish, aquatic invertebrates or algae. However, direct overspray or excess spray drift or runoff may be hazardous to aquatic plants, such as *Lemna gibba* (duckweed). Direct overspray is unlikely, as aerial application of the substance is forbidden on the label. In practice, the aquatic hazard from spray drift is likely to be acceptable, assuming lower drift and greater water depth than those for worst case analysis, and split application of the substance together with the low proportion of a catchment area likely to be treated at one time minimise the runoff hazard from rain. Suitable label warnings have been recommended to minimise the risk of aquatic contamination.

Efficacy and safety aspects

The efficacy data provided demonstrated that when applied to very young blackberry nightshade the product was able to provide significant suppression together with some weed mortality. Other minor weeds also listed on the label are also effectively controlled at a commercially acceptible standard.

Significant crop and non target crop phytoxicity was not observed during any of the trials conducted. However the label does indicate that temorary chlorosis may occur if the crop is under stress and gives instruction on how to reduce such instances.

Tomatoes and potatoes are the only crops which can be safely grown after a tomato crop which has been applied with Titus. Data provided on recropping intervals for other crops was regarded as not being sufficient to justify the proposed label recropping intervals. As such the applicant has amended the label to include sufficiently long recropping intervals (minimum 18 months) to allow further trials to be undertaken.

INTRODUCTION

This publication provides a summary of the data reviewed and an outline of the regulatory considerations for the proposed registration of the chemical rimsulfuron as a herbicide for the suppression of Blackberry nightshade and control of certain other broadleaf weeds in processing tomato crops.

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

Copies of full technical evaluation reports on rimsulfuron, covering toxicology, occupational health and safety aspects, environmental impacts and residues in food, are available from the NRA on request (see order form on page 33). They can also be viewed at the NRA library located at the NRA's offices, Level 1, Computer Associates House, 10 National Circuit, Barton ACT 2604.

Written comments should be received by the NRA by **21 October 1998**. They should be addressed to:

[redacted]

[redacted] [redacted]
[redacted]

Applicant

DuPont (Australia) Limited.

Product details

Rimsulfuron will be marketed under the trade name DuPont Titus® herbicide containing 250 g/kg rimsulfuron as dry flowable, water dispersable granule.

The product DuPont Titus® herbicide is fully formulated in France, then imported, repacked and relabelled in Australia.

DuPont (Australia) Limited intend to market DuPont Titus® herbicide in all states and territories. Rimsulfuron is currently registered in the USA and European Economic Community.

Chemistry and Manufacture

Active constituent

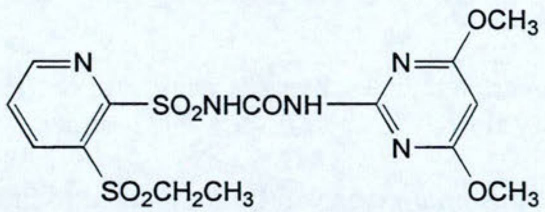
The chemical active constituent rimsulfuron has the following properties:

Common name (ISO):	rimsulfuron
Chemical name:	
IUPAC	N[[(4,6-dimethoxypyrimidin-2-yl)amino] carbonyl]-3-(ethylsulfonyl)-2-pyridinesulfonamide
CAS Registry Number:	122931-48-0
Empirical formula:	$C_{14}H_{17}N_5O_7S_2$
Molecular weight:	431.1
Physical form:	powder at ambient temperature
Colour:	white
Odour:	paste like
Melting point:	176-178°C
Density:	0.784

Octanol/water partition coefficient (P_{OW}):

	pH 5 buffered	1.94
	PH 7 buffered	0.0344
Vapour pressure at 25°C:	1.5×10^{-8} hPa	

Structural formula:



METABOLISM AND TOXICOKINETICS ASSESSMENT

Evaluation of toxicology

The toxicological database for rimsulfuron, which consists primarily of toxicity tests conducted using animals, is 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. Findings of adverse effects in any one species do not necessarily indicate such effects might be generated in humans. From a conservative risk assessment perspective however adverse findings in animal species are assumed to represent potential effects in humans unless convincing evidence of species specificity is available. Where possible, considerations of the species specific mechanisms of adverse reactions weigh heavily in the extrapolation of animal data to likely human hazard. Equally, consideration of the risks to human health must take into account the likely human exposure levels compared with those, usually many times higher, which produce effects in animal studies. Toxicity tests should also indicate dose levels at which 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

In rats, following oral dosing, rimsulfuron is rapidly eliminated in urine and faeces with very low residual levels in body tissues. Analysis of urine and faeces for metabolites revealed that unchanged rimsulfuron was the major component in both (over 50%).

Acute Studies

Technical rimsulfuron has low acute oral (LD_{50} >5000 mg/kg in mice and rats), dermal (LD_{50}>2000 mg/kg in rabbits) and inhalational (LC_{50}>5400 mg/m^3 in rats) toxicity. It is not a skin irritant in rabbits or a skin sensitiser in guinea pigs but is a moderate eye irritant in rabbits. Du Pont Titus Herbicide has low acute oral (LD_{50} >5000 mg/kg in mice and rats), dermal (LD_{50}>2000 mg/kg in rabbits) and inhalational (LC_{50}>7500 mg/m^3) toxicity. It is a moderate eye irritant in rabbits but has no skin irritant or skin sensitising properties in rabbits or guinea pigs, respectively.

Short-Term Studies

Groups of mice and rats were given 10 doses of rimsulfuron at 2200 mg/kg/dose orally over 2 weeks. There were no deaths in either species and the only compound-related effect was increased liver weight in mice after 14 days recovery, and in rats at the end of dosing (but not after recovery). Kidney weight was also increased for rats after 14 days recovery.

Mice were given rimsulfuron in the diet at doses up to 1575 mg/kg/day for 90 days. There were no deaths and adverse findings were minimal and confined to minor reductions in weight gain, an increase in red blood cells and haemaglobin, and increased liver weights (confined to the highest dose).

Rats were given dietary doses of rimsulfuron at up to 1622 mg/kg/day for 90 days. At doses of 120 mg/kg bw/day and above rats ate less and gained less weight. White blood cells were decreased in animals at 600 or 1600 mg/kg bw/day. Rimsulfuron increased the urinary output of females at the highest dose. Liver weights were increased at 600 and 1600 mg/kg bw/day with some evidence of enlarged liver cells.

Dogs were given rimsulfuron in the diet at doses up to 680 mg/kg/day, for 90 days. There were no clinical signs related to treatment. Animals at 190 or 680 mg/kg bw/day tended to eat less and gain less weight. At doses above 190 mg/kg bw/day, there were a number of effects due primarily to altered liver, and possibly altered kidney function (increased alkaline phosphatase. cholesterol, globulin, phosphate, total protein and sodium; and decreased albumin, calcium, blood urea and aspartate amino transferase). Rimsulfuron increased urine flow (diuretic effect) at and above 190 mg/kg bw/day. Liver and kidney weights were increased and heart weights were decreased, at 190 and 680 mg/kg bw/day.

Long-Term Studies

Mice were given dietary rimsulfuron at doses up to 1500 mg/kg/day for eighteen months. Clinical signs were minimal with no evidence of carcinogenicity. More females at 1500 mg/kg bw/day had cataracts and hair loss than was seen in control groups. Decreased bodyweight and bodyweight gain was seen at 1500 mg/kg bw/day and increased liver and testes weights, and a decrease in kidney weight, were seen for males, with increased liver, heart and kidney weights observed in females. At the highest dose some degenerative changes in the testis were more common (testicular artery and tunica).

Rats were given rimsulfuron in the diet at doses of up to 570 mg/kg/day for 2 years. Animals at the highest dose lost weight, or gained less weight, at periods during the study. Males at 120 mg/kg bw/day lost weight also. At the end of the study period, liver weights were increased at 120 and 415 mg/kg bw/day for males and at 570 mg/kg bw/day for females, but liver histology was normal. Rimsulfuron was not carcinogenic. The changes observed in the liver were consistent with a normal adaptive response to an increased burden of a foreign chemical.

Dogs were given dietary rimsulfuron at doses up to 360 mg/kg bw/day for one year. There were no deaths and clinical signs were minimal and unrelated to treatment. Opacities in the cornea of the eye were seen in two females and one male at the highest dose. Microscopic examination of the corneal opacities confirmed the cause as lipid accumulation, most likely secondary to altered liver function. Females at the highest dose gained less weight and both sexes at this dose level had increased white cell counts. At 82 mg/kg bw/day and above, there were changes consistent with altered liver function (increased cholesterol and alkaline phosphatase levels). Urine volume was increased at the highest dose. Kidney and liver weights were increased from 82 mg/kg bw/day but there were no microscopic changes in the liver. Microscopic examination revealed some testicular degeneration in half the males at 82 and 320 mg/kg bw/day. A slight increase in cell numbers (hyperplasia) was observed in the lining of the trachea in the majority of animals at the highest dose.

Reproduction and Developmental Studies

In a one generation pilot study in rats fed rimsulfuron in the diet at up to 1622 mg/kg/day, no evidence of adverse effects on reproduction or lactation were noted. In the subsequent two generation study, rats were fed rimsulfuron at up to 1126 mg/kg/day for males and 1316 mg/kg/day for females. Adults at the highest dose levels ate less and gained less weight. The health of treated animals was otherwise unaffected by treatment, and mating and fertility were normal in each generation. The second generation of pups had lower weights at the highest dose level and the number of litters containing a pup of below normal size was increased. No treatment related deformities were observed in either generation.

Rimsulfuron was given orally to mated female rats at doses up to 6000 mg/kg bw/day during foetal organ formation. Animals at 6000 mg/kg ate less and gained less weight during treatment but had normal weights by the end of the study. The health of the animals was otherwise unaffected and foetal development was normal. At the highest dose a slight increase in the incidence of delayed bone formation, reflecting the slight maternal toxicity, was observed.

Rimsulfuron was given orally to artificially inseminated rabbits at doses up to 1500 mg/kg bw/day during foetal organ formation. One rabbit died at 500 mg/kg bw/day and most at 1500 mg/kg bw/day. Rabbits treated at 500 mg/kg bw/day ate slightly less but had normal weights. Most of the animals that died were bleeding in the stomach but there were no other dose-related findings. Two rabbits aborted at 500 mg/kg bw/day and three at 1500 mg/kg bw/day but no effects were seen on foetal survival or number of live fetuses per litter. There was no effect on mean fetal bodyweight and no compound-related external, internal organ or skeletal malformations.

Genotoxicity

Rimsulfuron was not genotoxic in a range of tests using bacterial (Ames test), mammalian (rat liver UDS, Chinese hamster ovary cells) and human cells (lymphocytes).

Public health standards

Poisons Scheduling

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

The NDPSC recommended that formulations containing rimsulfuron be placed 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.

NOEL/ADI

The most sensitive species tested was the dog with a NOEL of 1.6 mg/kg bw/day in a 12 month study. In order to calculate an Acceptable Daily Intake (ADI) for humans, a safety factor is applied to the NOEL in the most sensitive species. The magnitude of the safety factor is selected to account for uncertainties in extrapolation from animal data to humans, variation within the human population, the quality of the experimental data, and the nature of the potential hazards. Using a safety factor of 100, an ADI of 0.02 mg/kg bw/day was established for rimsulfuron.

RESIDUES ASSESSMENT

Introduction

DuPont Titus® herbicide is used for the suppression of Blackberry Nightshade and control other broad-leaf weeds in tomatoes being grown for processing, particularly when the tomatoes are young. The product is not to be used on greenhouse tomatoes. The Blackberry Nightshade is currently removed by chipping when the tomatoes begin to flower. There are stated to be no alternatives to chipping other than the proposed use of the Titus product. The active is the new chemical, rimsulfuron, present at 250 g/kg. Residue data, tomato and animal metabolism studies, and environmental fate and chemistry data were considered in the residue evaluation of the application.

Background

Rimsulfuron is a post-emergence sulfonylurea herbicide intended for use in Australia to control certain broadleaf weeds in tomatoes being grown for processing. Rimsulfuron is a selective systemic herbicide which is absorbed by foliage and roots. It inhibits the plant enzyme, acetolactate synthase, which results in cell growth and division being stopped.

Metabolism

In rats rimsulfuron was readily absorbed and rapidly eliminated via the urine. The majority of the recovered radioactivity in urine and faeces was intact rimsulfuron. Tissue results showed no fat deposition occurred and that total radioactivity levels in muscles were low. Liver and kidney contained measurable total residues.

A lactating goat study showed rimsulfuron was readily eliminated in the urine and faeces with very little tissue retention. No detectable residues were found in milk, fat, or muscle and low residue levels found in kidney and liver were not identified as parent or known metabolites. The rapid excretion and lack of significant uptake by tissues at a feeding level of about 10 ppm for 3 days indicated residues in ruminants should not be an issue when Titus is applied to tomatoes, especially as feeding of processed tomato waste to cattle, etc. has not been identified as significant and residues in the waste etc. are expected to be non-measurable.

In hens fed rimsulfuron at about 10 ppm in the diet for four days, rimsulfuron was eliminated in the excreta relatively quickly and at a fairly constant rate. Rimsulfuron was present as a major residue component in the excreta along with rimsulfuron degradation products. Residues in eggs, fat, and muscle were <0.02 ppm. In kidney and liver, rimsulfuron was present at levels of 0.01-0.05 ppm. The lack of significant uptake of residues by the poultry tissues after short-term feeding at up to 10 ppm indicated that feeding of treated tomato produce to poultry should not be a major residue issue as residues in tomatoes and processed tomato products and waste are expected to be non-measurable.

A tomato metabolism study showed that rimsulfuron residues readily dissipated from tomato foliage after field application and that no residues were in or on the tomatoes, even at exaggerated treatment rates. Seven days after application, tomato foliage contained no rimsulfuron residues and metabolite residues steadily dissipated from levels of 0.02 to 0.24 ppm (at 7 days after treatment) to be ≤0.09 ppm 60 days after treatment.

The metabolic pathway in the rat, goat, hen and tomato were considered similar with bridge contraction a major route of degradation along with some sulfonylurea cleavage. The studies did not identify rimsulfuron or its metabolites as fat soluble.

Analytical methods

Analytical methodology to determine rimsulfuron was based on a method which used an HPLC chromatographic clean-up followed by an HPLC quantitation with UV detection. The method took advantage of the change in retention of rimsulfuron as a function of pH to separate it from co-extractives. The average recovery for corn samples was of the order of 77-89% at fortification levels of 0.05 to 0.5 ppm with a limit of quantitation of 0.05 ppm. When used in the Australian tomato residue trials, recoveries were higher than normally considered acceptable. This may point to some need for laboratories performing the analyses to refine their techniques. The methodology would appear adequate to identify and quantitate rimsulfuron residues in or on tomatoes.

Storage stability

A US storage stability study on rimsulfuron residues in tomatoes showed that rimsulfuron residues were stable for up to 6 months when stored at -20°C ± 5°C

Residue definition

The plant metabolism studies and analytical methodology support a residue definition of "rimsulfuron" as being appropriate and relevant. Such a definition is adequate to measure compliance with good agricultural practice.

Residue trials

Five Australian tomato residue trials were presented. Tomato foliage residue data were presented with two of these trials. In general the trials were conducted at rates greater than proposed and tomatoes were sampled over periods of 10 to 104 days. In all cases rimsulfuron levels were reported as <0.05 mg/kg. Supplementary US data on tomatoes given two rimsulfuron treatments of approximately 2 and 4.6 times the proposed Australian rates were also presented. There were generally 14 days between the US applications and tomatoes were harvested at 0 to 4 days or 40 plus days after treatment. In all cases rimsulfuron residues were <0.05 ppm. Taken as a whole, the residue data support the applicant's proposed MRL of *0.05 mg/kg for rimsulfuron in tomatoes with a four week harvest withholding period.

Processing studies

Because of the absence of any rimsulfuron residues in treated tomatoes, processing studies have not been considered necessary at this time.

Animal feed commodity MRL

The limited tomato forage residue data presented in the Australian trials indicates that with a 40 day period between treatment and sampling, tomato forage is not expected to have measurable rimsulfuron residues present. This conclusion is reached on the basis of results from treatments at rates exceeding the proposed Australian treatment rate. In a study conducted at the Australian proposed rate of 60 g Titus/ha, a rimsulfuron concentration of 0.24 mg/kg in tomato forage was reported. Because the higher treatment rates in the study did not indicate any residues in the forage, the 0.24 mg/kg result has not been considered validated at this time.

On the basis of the expectation of there being no measurable residues in tomato fodder or forage, the decision was taken that the applicant's proposed fodder/forage MRL would be of little value and consequently, would not be required. However, there is the occasional occurance when crops are surplus to requirements sheep and cattle are put into graze. Residue data provided demonstrated that residues were non-detectable in tomato forage at 40 days after treatment when applied at rates exceeding the recommended maximuim rate As such a grazing/feeding withholding period for tomato fodder and forage was set at 6 weeks.

Animal commodity MRLs

The applicant has proposed meat (mammalian), edible offal (mammalian), and milks MRLs of *0.01 mg/kg respectively. On the basis of there being no measurable residues in tomato processing waste or tomato forage or fodder and the animal metabolism results, there is little expectation of residues in animal commodity residues after feeding of treated tomato forage, fodder, or processing waste. However no analytical method to determine rimsulfuron residues in animal commodities has been presented nor has there been strong reason made for recommending animal commodity MRLs. Consequently it was decided to make no recommendations on rimsulfuron animal commodity MRLs at this time.

Estimated dietary intakes

The theoretical maximum daily intake of rimsulfuron from the proposed use is approximately 0.5% of the rimsulfuron ADI of 0.02 mg/kg body wt/day.

Bioaccumulation potential

The K_{ow} values of <2 reported for rimsulfuron mean that fat solubility of the parent is expected to be low. The animal metabolism studies support this. The polar natures of the degradation products also point to little tendency for fat solubility or accumulation.

Recommendations

Registration of the product:

Registration of DU PONT TITUS™ HERBICIDE for use on tomatoes for processing is supported on residue grounds.

Recommended Amendments to the MRL Standard:

Table 1

Compound	Food	MRL (mg/kg)
ADD		
Rimsulfuron		
VO 0448	Tomato (for processing)	*0.05

Table 3

Compound	**Residue**
ADD	
Rimsulfuron	Rimsulfuron

The MRL recommendations indicated above will be conveyed to the National Food Authority (NFA) for consideration for incorporation into *Standard A14* of the Food Standards Code and consequent adoption into the State/Territory food legislation.

Withholding periods:
The following statement is recommended to help ensure residue levels in treated tomatoes are acceptable:

DO NOT APPLY LATER THAN 4 WEEKS BEFORE HARVEST.

The following statement is recommended to help ensure residue levels in treated forage and fodder are acceptable:

DO NOT GRAZE OR CUT FOR STOCK FOOD FOR 6 WEEKS AFTER APPLICATION

ASSESSMENT OF OVERSEAS TRADE ASPECTS OF RESIDUES IN FOOD

Trade

Establishment of rimsulfuron residues in tomatoes or processed tomato products at or about the limit of quantitation of 0.05 mg/kg would not be expected to result in trade issues. No Codex Alimentarius Commission MRLs have been established for rimsulfuron. A US temporary tomato tolerance of 0.1 ppm has been established for rimsulfuron. A Spanish tomato MRL of 0.05 mg/kg has been reported established. Animal commodities are not expected to have measurable rimsulfuron residues arising from the proposed use pattern or feeding of tomato waste etc.

Risk assessment and management

The proposed use pattern and residue results indicate that it is unlikely there will be measurable rimsulfuron residues in treated tomatoes grown for processing when a 4 week harvest withholding period is applied. Because of the "nil" residue situation, the risk of unacceptable residues in tomatoes, tomato processing waste, tomato fodder and forage and, consequently, animals fed treated produce is considered low. Adherence to the proposed use pattern, especially its harvest withholding period would be expected to effectively manage the residue risk identified with this proposed use.

The USA has established a temporary tomato tolerance of 0.1 ppm which is of similar magnitude to the *0.05 mg/kg MRL recommended for Australia. The US has not established animal commodity tolerances for rimsulfuron. The expectation that residues in animal commodities arising from the proposed use should be negligible provide further confidence that the residue risk associated with the proposed use of rimsulfuron have been identified and is controllable.

Occupational Health and Safety Assessment

Rimsulfuron is not listed as a hazardous substance in the NOHSC List of Designated Hazardous Substances. It is not determined to be a hazardous substance according to NOHSC Approved Criteria for Classifying Hazardous Substances.

Rimsulfuron is a white powder with faint, ester like, odour. Technical rimsulfuron is of low acute toxicity by all routes. It is not a skin irritant in rabbits or a skin sensitiser in guinea pigs, but is a moderate eye irritant in rabbits.

DuPont Titus® herbicide (Titus) cannot be determined to be a hazardous substance, based on NOHSC criteria. It is a dry flowable water dispersible granule formulation that is not expected to be dusty. Titus has low acute toxicity by all routes. It is a moderate eye irritant in rabbits, but has no skin irritant or skin sensitising properties in rabbits and guinea pigs, respectively.

The product will be imported fully formulated in 200 g jars.

Formulation, repackaging, transport, storage and retailing

Considering that the product will be imported formulated, transport workers, store persons and retailers will only handle the packaged product; therefore, they could only become contaminated if the packaging were breached.

Advice on safe handling of the product during routine use is provided in the MSDS for Titus.

End use

Titus is to be applied to young actively growing weeds, eg. Blackberry Nightshade from cotyledon to 2 leaf stage and other weeds from cotyledon to 4 leaf stage. It is diluted in water, mixed with a non-ionic surfactant, and applied as a ground spray. The application rate is 60 g product/ha in 50 L/ha, minimum spray volume (0.12% w/v Titus, 0.03% rimsulfuron). Aerial application and use in greenhouse tomatoes is prohibited on the product label.

Sequential applications, not exceeding 150 g product/ha, are recommended with at least 7 to 14 days between the two applications. The product may be applied as a full field treatment or directed band spray. A Restricted Entry Period is not specified on the draft label; the Withholding Period for harvest is 4 weeks.

Exposure of end users will be predominantly through the dermal route during mixing/loading, ground application and clean-up procedures. Inhalation exposure to spray mist may occur; the product is non-volatile and not expected to be dusty; therefore, inhalation exposure to vapour or dust is not expected to be significant. The undiluted product is a moderate eye irritant; given the high dilution of product in the working strength solution (0.12% w/v), the prepared spray is not expected to be irritant to the eyes. Workers re-entering treated crops may come into contact with product residues.

No worker exposure data was available for rimsulfuron or Titus. The risk assessment was based on exposure estimates from two models, PHED and UK POEM. The risk assessment conducted using data from both models indicated that the risk was acceptable for mixer/loaders, applicators, and workers performing combined tasks wearing long pants and long sleeved shirts with and without gloves.

In addition, workers are required to wear a face shield or goggles, when opening the container and preparing the spray.

Entry into treated areas or handling treated crops

Limited residue data indicated that detectable foliar residues were found on the day of application only. Workers are not likely to re-enter tomato crops immediately after spray application. Therefore, a re-entry period is not recommended at this stage.

Recommendations for safe use

Workers involved in transport, storage, and retailing should be protected by safe work practices and training. End users should follow the instructions and Safety Directions on the product labels. Safety Directions include the use of face shield or goggles when opening the container and preparing the spray.

The Personal protective Equipment (PPE) recommended should meet the relevant Standards Australia:

AS 1337-1992 Eye Protection for Industrial Applications.

Manufacturers and importers should produce a MSDS for hazardous products containing rimsulfuron. These should contain information relevant to Australian workers, as outlined in the NOHSC National Code of Practice for the Preparation of Material Safety Data Sheets. Employers should obtain the MSDS from the supplier and ensure that their employees have ready access to it.

Conclusions

DuPont Titus® herbicide can be used safely if handled in accordance with the instructions on the product label. Additional information is available on the MSDS for DuPont Titus® herbicide.

ENVIRONMENTAL ASSESSMENT

Introduction

Du Pont (Australia) Ltd has applied for clearance and registration of the end-use product DuPont Titus® herbicide, containing the new active ingredient rimsulfuron (250 $g.kg^{-1}$ water dispensable granule formulation), as a post-emergent herbicide for use in young processing tomato crops. Rimsulfuron is a sulfonylurea herbicide, acting by inhibiting the plant enzyme acetolactate synthase, hence stopping cell division and plant growth by blocking branched chain amino acid biosynthesis. In common with other sulfonylurea herbicides, the means of crop selectivity is rapid metabolic inactivation in the crop.

Environmental Fate

It is proposed that DuPont Titus® herbicide will be applied in two applications 7-14 days apart, once per season to young tomato crops, at a maximum total rate of 150 g product/ha (37.5 g ai/ha), though the recommended application method (split application at 60 g product/ha on each occasion) actually results in a total of 120 g product/ha (30 g ai/ha). It is expected that the product will be applied by boomspray and the extent of spray drift should therefore be limited by application relatively close to the ground surface. The label forbids aerial application.

Contamination of the soil compartment within the treated area will occur through direct application of the substance to the soil in the process of applying it to small weed seedlings. Direct overspray, spraydrift and runoff could potentially affect non-target areas.

Hydrolysis

A hydrolysis study with rimsulfuron indicated that the rate of hydrolysis in the dark at ~25°C was very rapid at pH 9 ($t_{1/2}$ = 4.2-10.9 hours) and fairly rapid at pH 5 ($t_{1/2}$ = 4.5-4.7 days) and pH 7 ($t_{1/2}$ = 7.1-7.3 days). The major metabolic pathway for hydrolysis was shown to be contraction of the sulfonamide bridge to form a substituted urea (pH 5) or amine (pH 7 and pH 9) rather than the expected bridge cleavage, which was only a minor pathway. Similar rates of hydrolysis at these pHs were indicated in non-irradiated samples in an aqueous photolysis study. A separate hydrolysis study to different protocols indicated half lives of 1.5 days, 24.7 days and 14.8 hours at pH 5, 7 and 9 respectively at a nominal temperature of 22°C, indicating much slower degradation at pH 7 than the above study. The likely explanations for the longer hydrolysis half-life at nominal pH 7 in the latter study is that the pH in this study was maintained close to pH 7, but rose to pH 7.6 in the other study (hastening hydrolysis), and that the temperature was slightly cooler where the half-life was longer.

Photolysis

An aqueous photolysis study with rimsulfuron (with two different radiolabels) under initially sterile conditions found that the rate of degradation of this substance in water may be greater in light at pH 5 ($t_{1/2}$ with sunlight exposure 1.1 days, compared to 4.7 days in the dark), but not at pH 7 or 9 ($t_{1/2}$ 11-12.4 days and 10.2-12 hours, respectively, with sunlight exposure, and 6.4-6.5 days and 6.6-14.6 hours, respectively, in the dark). In air-dry, non-sterile soil, the rate of degradation of rimsulfuron (again with two different radiolabels) in a soil photolysis study was not affected by sunlight exposure ($t_{1/2}$ 11-12 days with and without sunlight exposure). With and without sunlight exposure, similar major metabolites were found in both studies to those found in a hydrolysis study with rimsulfuron under similar pH conditions, and it is likely that the principal initial means of degradation in both the photolysis studies was hydrolysis. However, in both water and soil, sunlight exposure led to the formation of polar substances not detected in non-irradiated samples, nor in the hydrolysis study, thus photolysis presumably assists the degradation of the major metabolites of rimsulfuron.

Degradation in soil and water

Aerobic and anaerobic soil metabolism

Studies show that hydrolysis appears to be important in the aerobic and anaerobic degradation of rimsulfuron in soil, the rate of degradation being affected by soil moisture content and a similar range of metabolites being produced. Aerobic soil metabolism studies in four soils indicate that the initial DT50 (1-2 months incubation) of rimsulfuron in soil incubated at 20-25˚C is in the range 20-60 days (fairly degradable), but degradation then appears to slow, with DT50s for 2-12 months in the range 60-180 days (slightly degradable). When one soil was incubated at 60% rather than 40% of maximum soil water holding capacity, the half life fell from 25 to 5 days, and when another soil was incubated at 10˚C rather than 20˚C, the half life rose from 30 to 77 days. Major metabolites found were the same substituted urea and amine bridge contraction products found in hydrolysis studies, representing ~32% and ~22% of applied radioactivity, respectively, after 12 months incubation, the urea having peaked at ~54% of applied radioactivity after 2 months incubation. Bridge cleavage products were formed to a lesser extent and evolution of $^{14}CO_2$ and other volatiles occurred to only a minor extent (< 7% of applied radioactivity) during the study period.

Because they are present in various soil and water degradation studies for up to several months at significant concentrations relative to the initial concentration of the parent substance, the toxicity of both the bridge contraction products should be considered in evaluating the overall environmental hazard from rimsulfuron.

In one of the above studies, samples were incubated under anaerobic conditions (excess water and nitrogen purging) for up to 2 months, after 10 days initial incubation under aerobic conditions. Half lives calculated for the anaerobic period were 18-24 days and similar metabolites were produced, but the amine bridge contraction product was produced at a faster rate (peak 56% of applied radioactivity, at the end of the study).

Aerobic aquatic metabolism

Studies of the rate of degradation of rimsulfuron in pond water at moderately alkaline pH (pH 7.8-8.4) under sterile or non-sterile conditions indicated half lives of 0.4-2.1 days at 25˚C and 48-77 days at 5˚C. At 25˚C, parent compound and the substituted urea bridge contraction product were undetectable after 10 days, whereas the concentration of the amine bridge contraction product reached > 90% of applied radioactivity by 7 days incubation, before falling to 61-75% of applied radioactivity after 6 months incubation. As with the aerobic and hydrolysis studies, cleavage of the sulfonyl bridge was a relatively minor degradation pathway. Under non-sterile conditions, cumulative $^{14}CO_2$ evolution reached ~8-10% of applied radioactivity after 6 months The results suggest that the initial degradation of rimsulfuron in pond water was by hydrolysis, which was rapid under these pH conditions, but that microbial degradation was important in converting the initial metabolites to CO_2, this mineralisation process occurring relatively slowly.

In a water/sediment biodegradation study where the water and sediment of two different systems (low and high sediment organic matter content) were initially at pH 5-7, the half life of rimsulfuron in the whole system was 5.2-6.2 days at 20-25°C. Similar metabolites to the pond water study were produced, but little $^{14}CO_2$ was produced in the 3 months of this study. After 89 days incubation, ~54% and ~21% of applied radioactivity, respectively, was found in the high and low organic matter content sediments(12.8% and 1.2% OM, respectively).

Mobility

Evaluation of the soil mobility properties of rimsulfuron and its principal degradates using a thin layer chromatography procedure with four different soils indicated that rimsulfuron is intermediate to very mobile, mobility being greatest in the soil lowest in organic matter content and lightest in texture. Major metabolites of rimsulfuron (bridge contraction metabolites and metabolites from aged soil) were all lower in mobility than the parent compound. Conventional batch equilibrium studies of adsorption and desorption of rimsulfuron in four soils found organic carbon adsorption constants (K_{oc}) of 18.9 to 63.0 (average 46.7) for rimsulfuron, rating it as having high (K_{OC} = 50-150) to very high (K_{OC} = 0-50) mobility in soil. Adsorption was reversible, rimsulfuron being moderately desorbed from all four soils.

High mobility of rimsulfuron in soil was also indicated in a leaching study where ^{14}C-labelled rimsulfuron was applied freshly to columns of four different soils, or aged soil (10 days incubation) applied to the soil column of one of the soils, followed by leaching with the equivalent of 200 mm water over 48 hours. A high proportion (57-98%) of the applied radioactivity was recovered in eluates where rimsulfuron had been freshly applied, more so in the two soils lowest in organic matter (1.2-1.3% OM), but only 29-42% of applied radioactivity was recovered in eluate from aged soil. In three of the soils where rimsulfuron was applied freshly, >50% of the residues in eluate were present as rimsulfuron, whereas metabolites dominated in the other soil and where aged soil was applied.

Environment Australia comments that the results suggest that metabolites may also be somewhat mobile, but notes that at least some of the metabolites measured may have formed directly in the eluate rather than eluting from the column.

Calculations by Environment Australia of the Gustafson Ubiquity Score (GUS) using the available K_{OC} and half-life data indicate that rimsulfuron is a "probable leacher" (GUS > 2.8) under conditions where it degrades relatively slowly, to an "improbable leacher" (GUS < 1.8) under conditions where breakdown is relatively rapid. Moist conditions favouring leaching are also likely to favour rapid degradation, hence rimsulfuron is unlikely to reach groundwater and if it did, would continue to dissipate by hydrolysis. A Pesticide Root Zone Model assessment of groundwater potential provided by the applicant produced a similar conclusion, predicting that soil water concentrations of rimsulfuron reaching a depth of 1 metre would be < 0.001 ppb. Rimsulfuron is only very slightly volatile and unlikely to mobilise significantly by this means, as shown by a volatility study with soil and dwarf runner beans supplied by the applicant.

Field dissipation

Experiments with rimsulfuron at four sites indicated field dissipation half lives for this substance of 5.4 to 9.6 days under warm conditions (mean soil temperature at 0-7.8 cm in the month following application ~23-24°C) and 15.9-17.7 days under cooler conditions (corresponding mean soil temperature ~14°C). At three of the sites the main metabolite found in the surface 7.8 cm of soil was the bridge contraction product IN-70941 (up to 26-50% of peak rimsulfuron concentration), and there were relatively low concentrations of IN-70942 (≤ 20% of peak rimsulfuron concentration), or the bridge cleavage products, IN-J290 and IN-E9260 (≤ 10% of peak rimsulfuron concentration). However, at one site IN-70942 became the predominant metabolite (up to 54-68% of peak rimsulfuron concentration, remaining at 35% of peak rimsulfuron concentration after 18 months).

Thus the rates of degradation and metabolites found in these field dissipation studies were consistent with laboratory soil metabolism studies, the dominance of IN-70942 at one site being similar to results in water or anaerobic soil. Limited downward movement of rimsulfuron or its metabolites was detected, residues only being found in the surface 15.2 cm of soil and peak concentrations of total radioactivity at 7.6-15.2 cm being 13-35% of those in the surface 7.6 cm. Less downward movement of rimsulfuron and its metabolites was found than might have been expected from soil adsorption/desorption or column leaching studies, but rainfall and irrigation in the first month after treatment were relatively low compared to the rate of water application in the leaching study, and residues may have been present below the limit of detection (~6-17 % of peak soil concentrations).

Accumulation in soil

Under the conditions of use early in the life of irrigated tomato crops, rimsulfuron is expected to degrade rapidly, with no detectable carryover from year to year, as found in field dissipation studies. Hence it is not expected to accumulate in soil, even with repeated annual use.

Bioconcentration/bioaccumulation

While no test has been provided, rimsulfuron or its metabolites are unlikely to bioaccumulate in fish as the toxicity, expected environmental concentration and frequency of use of the substance are very low. Furthermore, rimsulfuron is unlikely to persist in water ($t_{1/2}$ = ~8 hours to 7.3 days at 20-25°C, depending on pH) and its low octanol/water partition coefficient (K_{OW} < 2) suggest that it has a relatively low potential for accumulation in fish.

Results of a confined accumulation study of rimsulfuron in rotational crops were consistent with field dissipation studies with rimsulfuron, indicating rapid dissipation from soil and limited downward movement of rimsulfuron or its metabolites. Where residues were found at quantifiable levels in plant tissue, they declined with successively later planting (30 days, 120 days or 10 months after treatment) and did not include parent substance. Thus rimsulfuron should not accumulate in rotational crops grown in soil treated with the substance at field use rates.

Environmental Toxicity

Birds

Studies of the acute oral toxicity of rimsulfuron TGAC indicate that the LD50 from a single oral dose was > 2250 mg ai/kg bodyweight to bobwhite quail (*Colinus virginianus*) and > 2000 mg ai/kg bw to mallard ducks (*Anas platyrhynchos*). Studies of the acute oral toxicity of rimsulfuron 25DF, a formulation similar to that of DuPont Titus® herbicide, indicate that the LD50 from a single oral dose was > 2250 mg formulation/kg bw (> 562.5 mg ai/kg bw) to both bobwhite quail and to mallard ducks. Studies of the acute dietary toxicity of rimsulfuron 25DF indicate that the LC50 after 5 days exposure in the diet was > 5620 ppm formulation (1405 ppm ai) with both bobwhite quail and mallard ducks. These studies indicate that rimsulfuron TGAC is practically non-toxic (LD50 > 2000 mg ai/kg bw) to bobwhite quail and mallard ducks by acute oral exposure, that a 25DF formulation containing rimsulfuron was also practically non-toxic (LD50 > 2000 mg form/kg bw) to these species, and that the 25DF formulation was also practically non-toxic to bobwhite quail chicks and mallard ducklings by dietary exposure for 5 days (LC50 > 5000 ppm formulation in diet).

Aquatic Organisms

Fish

Acute (96 hour, static test for freshwater species and flow-through test for saltwater species) and chronic (21 day, flow-through test for trout and carp only) toxicity studies indicate that rimsulfuron TGAC and a 25DF formulation containing rimsulfuron (presumably similar to the proposed formulation for DuPont Titus® herbicide) are practically non-toxic (LC50 > 100 mg ai/L or 100 mg form/L, respectively) to various species of fish. Species tested in one or more studies included carp (*Cyprinus carpio*), rainbow trout (*Onchorynchus mykiss*), bluegill sunfish (*Lepomis macrochirus*) and sheepshead minnow (*Cyprinodon variegatus*). For each species, LC50 values were available for the TGAC based on mean measured concentrations over the study period, rather than nominal initial values.

Aquatic invertebrates

Acute (48 hour, static test for the daphnids and flow-through test for the saltwater species) and chronic (21 day, static renewal test for *D. magna* only) toxicity studies indicate that rimsulfuron TGAC and a 25DF formulation containing rimsulfuron (presumably similar to the proposed formulation for DuPont Titus® herbicide) are practically non-toxic (EC50 or LC50 > 100 mg ai/L or 100 mg form/L, respectively) to the daphnid species *Daphnia magna* and *Daphnia carinata*, the mysid shrimp, *Mysidopsis bahia*, and the eastern oyster, *Crassotrea virginica*. For each species except *D. carinata*, EC50 or LC50 values were available for the TGAC based on mean measured concentrations over the study period, rather than nominal initial values.

Diatoms, algae and aquatic plants

Tier 1 (single concentration) acute (5 day, static tests) with rimsulfuron and the freshwater green alga, *Selenastrum capricornutum*, the freshwater blue-green alga, *Anabaena flos-aquae*, and the marine diatom *Skeletonema costatum* indicated NOECs ≥ 29 µg ai/L, 35 µg ai/L and 48 µg/L measured initial concentrations, respectively. A similar Tier 1 test with the freshwater diatom, *Navicula pelliculosa*, found significant toxicity (≥ 25% inhibition to biomass and cell counts at test termination) from rimsulfuron TGAC at an initial measured concentration of 30 µg ai/L, but the EC50 was above this concentration. Less toxicity was evident when a Tier 2 test was conducted with measured initial concentrations up to 108.6 μg/L (NOEC = 108.6^{-1}: there was up to 31.6% inhibition in biomass relative to the combined control, but the difference was not statistically significant and no dose-response pattern was evident). An algistatic activity test (static) with *Selenastrum capricornutum* indicated EC50s for biomass production at 72 and 120 hours of 1.2 mg/L and 1.6 mg/L, respectively, and an EC50 for maximum growth rate (24-48 h) of 2.8 mg/L, indicating moderate toxicity based on nominal initial concentrations of the substance. This test found the effect of the substance on this species at the maximum test concentration of 10 mg/L to be algistatic, rather than algicidal.

However, a 14 day test (static) found rimsulfuron TGAC to be very highly toxic to the freshwater duckweed, *Lemna gibba* (MATC and EC50 for frond biomass dryweight = 0.97 and 11.6 μg/L, respectively; and MATC for number of fronds produced = 0.12 μg/L, based on nominal initial concentrations adjusted according to the available measured concentration data).

Terrestrial invertebrates and mammals

A 48 hour dietary study indicates that rimsulfuron TGAC is not hazardous to bees (*Apis mellifera*) by dietary exposure (LC50 > 700 ppm). Laboratory tests with a rate equivalent to 37.5 g ai/ha as a 25 WG formulation showed no significant effect on mortality of green lacewing (*Chrysoperla carnea*) larvae or of adults of the parasitic wasp *Aphidius rhopalosiphi*, nor on reproduction indices of surviving adult females subsequently (production of viable eggs per surviving female lacewing and parasitism success of female wasps). A 14 day study in artificial soil indicates that rimsulfuron TGAC is very slightly toxic to the earthworm species *Eisenia foetida* (LC50 > 1000 mg ai/kg soil). Summary data indicate that rimsulfuron is practically non-toxic to mammals (LD50 to rats and mice > 2000 mg/kg for both the TGAC and formulation).

Phytotoxicity

Rimsulfuron acts by inhibiting the plant enzyme acetolactate synthase, the means of crop selectivity being the rapidity of metabolic inactivation. Environment Australia assumes that there will be susceptibility to this substance among Australian native species and notes that the applicant has included strong cautions regarding phytotoxicity to non-target plants on the label.

Toxicity of major metabolites IN-70941 and IN-70942

The applicant states that IN-70941 had no significant biological activity in herbicide, insecticide, fungicide and nematicide screening tests. There is some indication that the major metabolites of rimsulfuron are not likely to be toxic at expected environmental concentrations in water in that many of the aquatic toxicity tests described were conducted under static test conditions, where the organisms tested were exposed to metabolites produced as rimsulfuron hydrolysed. Reports provided by the applicant indicate that the metabolites IN-70941 and/or IN-70942 are slightly toxic to practically non-toxic (LC50/EC50 > 10 mg/L) to fish (rainbow trout) and daphnids (*Daphnia magna*). IN-70941 was found to be at most moderately toxic (the NOEC was ≥ 8.9 mg/L) to the freshwater green alga *Selenastrum capricornutum*. IN-70942 was not toxic to duckweed (*Lemna gibba*) at a concentration similar to the worst case expected environmental concentration (the NOEC was ≥ 17.5μg/L).

Environmental hazard

Hazard to birds

Estimated concentrations resulting in a diet exclusively based on feed contaminated by the maximum proposed rate of the substance (which is unlikely) are 4.3 mg/kg and 1.9 mg/kg for quail and mallard duck, respectively. These worst case concentrations are well below the acute oral LD50s and 5 day dietary exposure NOECs for these species, hence rimsulfuron used in accordance with label recommendations is not likely to present a hazard to birds ingesting these residues.

Hazard to aquatic organisms

Direct overspray at a rate of 150 g product/ha of a lentic waterbody 15 cm deep would result in a worst case water concentration of 23 ppb (assuming split applications 1 week apart and a hydrolysis half-life of 24.7 days). This concentration is well below LC50s and EC50s for fish and aquatic invertebrates, and is also below NOECs for the freshwater alga *Selenastrum capricornutum*, freshwater blue-green alga *Anabaena flos-aquae* and marine diatom *Skeletonema costatum*. The situation is less clear with the freshwater diatom *Navicula pelliculosa*, where the NOEC by Tier 1 testing was < 30 ppb and that by Tier 2 testing was = 108.6 ppb.

Studies with the major degradation products of rimsulfuron confirm that toxic levels of both substances to aquatic organisms are above expected worst case environmental concentrations.

However, rimsulfuron is clearly hazardous to the aquatic plant species *Lemna gibba* (duckweed) with direct overspray. A hazard to *Lemna gibba* still remains with 10% spray drift reaching a 15 cm deep waterbody, or from runoff resulting in similar concentrations in dams or streams, but these hazards are mitigated by various factors, including lower drift expected from the equipment used, greater water depth in nearby waterbodies than the 15 cm worse case, split application of the product, and dilution of runoff by uncontaminated water once it leaves a treated field. Direct overspray is unlikely as aerial application is forbidden on the product label and appropriate label warnings have been included to avoid contamination of aquatic areas by spray drift or runoff. The label should also carries standard warnings against contamination of water with the product, spray mix or used containers.

Hazard to terrestrial invertebrates

Residues of rimsulfuron are not expected to be hazardous to terrestrial invertebrates such as honey bees, insect predators and parasites or earthworms due to the low toxicity of the active ingredient with dietary exposure to bees and soil exposure to earthworms, and lack of toxicity to green lacewing and a parasitic wasp species exposed to residues of the formulated substance at the maximum label rate. Furthermore, there would be limited exposure of these species to rimsulfuron, given its proposed use on young seedling tomatoes.

Hazard to non-target plants

Rimsulfuron is expected to be phytotoxic to certain species of native plants, the severity and permanency of any effects would presumably varying between species and with the timing and dose received. Direct overspray is unlikely in the absence of aerial application, but non-target plants in the vicinity of the treated crop or drainage areas could be reached by spray drift or runoff. Appropriate label warnings should be included to minimise the risk of phytotoxicity occurring from these sources.

Conclusions

Environment Australia has assessed data in support of DuPont Titus® herbicide and believes that the application contains adequate environmental fate and toxicity data to demonstrate that the use of this product for control of weeds in processing tomatoes according to the label and good agricultural practice is unlikely to result in harmful effects on environmental organisms.

The greatest environmental hazard from use of the product is to aquatic plants as a result of direct overspray, spray drift or runoff reaching aquatic areas, but aerial application is forbidden and suitable label warnings have been included on the product label to minimise the likelihood of aquatic contamination.

EFFICACY AND SAFETY ASSESSMENT

Justification for use

Blackberry nightshade is a serious weed of processing tomato production, as it is taxonomically close to the crop, competes strongly with young plants, and currently has no selective herbicides available for chemical control. DuPont Titus herbicide provides sufficient suppression of this weed to substantially reduce its competitive effects provided there is follow up weed management. It could therefore result in significant savings for the farmer in weed control costs, especially for the labour intensive method of chipping. The efficacy of Titus against many other broadleaf weeds would also be a major commercial advantage to tomato producers.

Evaluation of efficacy

Data was presented from 15 small plot replicated trials conducted over three seasons and in a variety of sites in Victoria and NSW. This will adequately cover most of the environmental conditions under which the product will be commercially applied. Trial designs were adequate and the data has been analysed correctly

The data provided in the submission clearly indicated that, when applied to very young blackberry nightshade as according to the label directions, this weed is significantly suppressed in growth together with some weed mortality. The submission also demonstrated that other minor weeds listed on the label, and possibly others, are effectively controlled.

Due to the data only being able to demonstrate good suppression rather than full control of blackberry nightshade, the label claim has been restricted to - For the suppression of Blackberry Nightshade and the control of certain broadleaf weeds in tomatoes as per the directions for use table.

Safety to target and non-target species

Significant crop and non target crop phytoxicity was not observed during any of the trials conducted. However the label does indicate that temorary chlorosis may occur if the crop is under stress and gives instruction on how to reduce such instances. Tomatoes and potatoes are the only crops which can be safely grown after a tomato crop which has been applied with Titus.

The applicant provided label recropping recommendations from the USA as well as 2 Australian field trials as justification for the original recropping intervals of 6 months for wheat, barley and oats, and 11 months for sunflower, maize and zucchini. Unfortunately, the two Australian trials were subjected to abnormally wet conditions, hence severe water logging and resulted in poor crop emergence and growth. As such this was deemed not sufficient justification for the presented recropping intervals and further data has been requested to confirm the correct intervals.

The applicant has therefore amended the label to include the following recropping intervals to allow sufficient time to undertake the trials required:
Wheat, barley and oats – 18 months
Sunflower, maize and zucchini – 23 months.

"Label"

CAUTION

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

DUPONT

Titus®

herbicide

ACTIVE CONSTITUENT : 250 g/kg RIMSULFURON

GROUP	B	HERBICIDE

For the suppression of Blackberry Nightshade and control of certain broadleaf weeds in tomatoes as per the Directions for Use table.

IMPORTANT: READ THE ENCLOSED LEAFLET BEFORE USE.

Net contents 200 g

Du Pont (Australia) Limited
A.C.N. 000 716 469
168 Walker Street, North Sydney NSW 2060
(02) 9923 6111

Storage and Disposal

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

SAFETY DIRECTIONS

Will irritate the eyes. Avoid contact with eyes. When opening the container and preparing spray wear face shield or goggles. If product in eyes, wash it out immediately with water. Wash hands after use. After each days use wash face shield or goggles.

FIRST AID

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

For further information refer to the Material Safety Data Sheet.

IN A MEDICAL EMERGENCY CALL
1800 674 415 All hours

NOTICE TO BUYER

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

Batch No: NR A Approval No: 49213/1098
DOM

A00353343/10-98

"Leaflet"

CAUTION

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

Titus®

herbicide

ACTIVE CONSTITUENT : 250 g/kg RIMSULFURON

GROUP	B	HERBICIDE

COMPLETE DIRECTIONS FOR USE

THIS LEAFLET IS PART OF THE LABEL ATTACHED TO THE 200 g PACK.

® DuPont Registered Trademark

DIRECTIONS FOR USE

RESTRAINTS

DO NOT apply to plants wet with rain or dew.

DO NOT apply if rainfall is expected within 2 hours.

DO NOT apply to weeds that are not actively growing or stressed by any cause such as adverse weather conditions, drought, waterlogging. Broadleaf weeds under stress frequently become less susceptible to herbicide activity. This may result in an incomplete kill or only growth suppression.

DO NOT store a suspension of Titus® for more that two days, otherwise significant breakdown may occur.

DO NOT store tank mixes of Titus®.

DO NOT apply Titus® to greenhouse tomatoes.

SITUATION	WEEDS CONTROLLED	RATE	CRITICAL COMMENTS
Tomato (Processing)	Blackberry Nightshade (*Solanum nigrum*) Suppression only	60 g/ha followed 7 days later by 60 g/ha	Apply when the Blackberry Nightshade are at the cotyledon to 2 leaf stage. Split applications are necessary for maximum control. Good suppression rather than total kill will result.
	Caltrop (*Tribulus terrestris*) Paddy Melon (*Cucumis myriocarpus*) Heliotrope (*Heliotropium europaeum*) Musky Crowsfoot (*Erodium moschatum*) Charlock (*Sinapsis arvensis*) Sub-Clover (*Trifolium subterraneum*)		Apply when weeds are at the cotyledon to 4 leaf stage.
Always add non-ionic surfactant (1000 g/L - non buffering type) at 250 mL/100 L (0.25 % v/v) of final spray volume. The addition of crop oil concentrate may result in crop injury.			

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

WITHHOLDING PERIOD

TOMATOES : DO NOT APPLY LATER THAN 4 WEEKS BEFORE HARVEST
DO NOT GRAZE OR CUT FOR STOCK FOOD FOR 6 WEEKS AFTER APPLICATION

GENERAL INSTRUCTIONS

DuPont Titus® herbicide is for selective post emergent control of certain broadleaf weeds in tomatoes.

Best results are obtained when DuPont Titus® herbicide is applied to young actively growing weeds. The degree of control and duration of effect are dependent on rate used, sensitivity and size of target weeds and environmental conditions at the time of and following application.

DuPont Titus® herbicide stops growth of susceptible weeds rapidly. However, typical symptoms of dying weeds (chlorosis or discolouration) may not be noticeable for 1 to 3 weeks after application depending on the environmental conditions and susceptibility. Warm, moist conditions following treatment promote the activity of DuPont Titus® herbicide, while cold, dry conditions delay activity. Weeds hardened-off by cold weather and/or drought stress will be less susceptible.

A vigorously growing crop will aid weed control by shading and providing competition to weeds.

Crop Safety

Crop stress factors that occur during, prior to, or after the application may cause, temporary chlorosis (lime green colour) to occur. Symptoms usually disappear within 5 to 15 days. Drought, frost, cold temperatures, high temperatures, or extreme temperature variations can be stress factors. To minimise the potential for temporary chlorosis, it is recommended that Titus® be applied only if there have been at least 3 successive days of sunny weather prior to application.

Tomato varieties may differ in their response to various herbicides. When using Titus® for the first time on a particular variety, limit the initial use to a small area. If no symptoms of crop injury occur 7 days after treatment, the balance of the area can be treated.

Sequential Applications

Annual weeds at times may have multiple flushes of seedlings or treated perennials may sometimes regrow from underground stems or roots, depending on rainfall and other environmental conditions. To maximise control of such weeds, it is necessary to use a sequential application of Titus® in which the first application goes on early followed by a second application 7 days later.

Cultivation

In areas where cultivation is used, the ideal timing for cultivation is 10 to 14 days after the Titus® application.

Spray Preparation

DuPont Titus® herbicide is a dry flowable formulation to be mixed with water and applied as a spray. Partially fill the spray tank with water. Using the Titus® measuring cone provided, measure the amount of DuPont Titus® herbicide required for the area to be sprayed. Add the correct amount of DuPont Titus® herbicide to the spray tank with the agitation system engaged. Top up to the correct volume with water. THE MATERIAL MUST BE KEPT IN SUSPENSION AT ALL TIMES BY CONTINUOUS AGITATION.

In tank mixes, DuPont Titus® herbicide must be in suspension before adding the companion herbicide or surfactant/wetting agent.

Compatibility

DuPont Titus® herbicide is compatible with DuPont Lexone® DF herbicide and may be applied to tomatoes for broader spectrum weed control on weeds such as Fat hen, Hogweed (Wireweed), and Pigweed. *Refer to the DuPont Lexone® DF® label for Directions for Use*. However, when Titus® is tank mixed with Lexone® reduced efficacy on Barnyard grass can be expected. In cases where Barnyard grass is a major weed then an initial application of Titus® followed by a tank mix with Lexone® may be desirable. Consult a DuPont representative for further information or advice.

Titus® is compatible with methomyl formulations, when Titus® is tank mixed with Lexone® however some temporary chlorosis may be experienced with liquid formulations. Titus® is compatible with synthetic pyrethroid insecticides.

DO NOT mix Titus® with organophosphate insecticides, or fungicides. Allow 7 days between application of Titus® and a treatment using these products.

Use of Surfactant/Wetting Agent

Always add non-ionic surfactant (1000 g/L - non buffering type) at 250 mL/100 L (0.25 % v/v) of final spray volume. The addition of crop oil concentrate may result in crop injury.

Ground Spraying

Use a boom spray properly calibrated to a constant speed and rate of delivery to ensure thorough coverage and a uniform spray pattern. Avoid overlapping and shut off spray booms while starting, turning, slowing or stopping. Apply a minimum of 50 L prepared spray/ha.

DO NOT apply Titus® by air.

Sprayer Cleanup

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

1. Drain tank, then flush tank, boom and hoses with clean water for a minimum of 10 minutes.

2. Fill the tank with clean water then add 300 mL household chlorine bleach (containing 4% chlorine) per 100 L of water. Flush through boom and hoses then allow to stand for 15 minutes with agitation engaged, then drain.

3. Repeat step 2.

4. Nozzles and screens should be removed and cleaned separately. 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 fertiliser 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 and lung irritation. **DO NOT** clean equipment in an enclosed area.

Resistant Weeds Warning

GROUP	B	HERBICIDE

DuPont Titus® herbicide is a member of the sulfonylurea group of herbicides. DuPont Titus® herbicide has the inhibitor of acetolactate synthase (ALS) mode of action. For weed resistance management DuPont Titus® herbicide is a Group B herbicide.

Some naturally-occurring weed biotypes resistant to DuPont Titus® herbicide and other ALS herbicides may exist through normal genetic variability in any weed population. The resistant individuals can eventually dominate the weed population if these herbicides are used repeatedly. These resistant weeds will not be controlled by DuPont Titus® herbicide or other ALS herbicides.

Since the occurrence of resistant weeds is difficult to detect prior to use, DuPont accepts no liability for any losses that may result from failure of DuPont Titus® herbicides to control resistant weeds.

Large numbers of healthy surviving weeds can be an indication that resistance is developing. Efforts should be taken to prevent seed set of these survivors.

DO NOT use an ALS inhibitor herbicide against the same weed in the crop following the use of DuPont Titus® herbicide alone either as a fallow or pre-crop treatment or post emergent treatment.

Avoid the prolonged use of ALS inhibitor herbicides on the same weed population.

If the user suspects that an ALS inhibitor resistant weed is present, DuPont Titus® herbicide or other ALS inhibitors herbicides recommended for the control of that weed should not be used.

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

Crop Rotation Recommendations

The amount of Titus® which may remain in the soil is dependant on the rate used, soil pH and organic matter content, time elapsed since Titus® application, and climatic and weather factors. The most important breakdown factor is the amount of moisture (rainfall or irrigation) from time of the last application of Titus® to planting of the follow-on crop.

In the case of crop failure only tomatoes or potatoes can be resown.

Land previously treated with DuPont Titus® herbicide may be sown to any of the specified crops after the interval indicated in the following table:

Crops	**Minimum interval**
Wheat, barley, oats	18 months
Sunflower, maize, zucchini	23 months

Protection of Crops, Native and Other Non-Target Plants

This product may cause injury to or loss of trees and other vegetation, including aquatic plants. **DO NOT** apply spray or drain or flush equipment on or near trees or other plants or on areas where their roots may extend or in locations where the chemical may be washed or moved into contact with their roots. **DO NOT** apply under meteorological conditions or from spraying equipment which could be expected to cause spray to drift onto adjacent areas, including crops, non-target plants or aquatic areas, as injury may occur.

Protection of Wildlife, Fish, Crustacea and Environment

This product may affect algae and aquatic plants. **DO NOT** contaminate any waterway or body of water by spraying, cleaning of equipment or disposal of concentrated product, spray mix or used containers.

Storage and Disposal

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GLOSSARY

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

References

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

National Registration Authority for Agricultural and Veterinary Chemicals 1997, *Ag Requirements Series: Guidelines for Registering Agricultural Chemicals*, NRA, Canberra.

National Registration Authority for Agricultural and Veterinary Chemicals 1996, *MRL Standard: Maximum Residue Limits in Food and Animal Feedstuffs*, NRA, Canberra.

National Registration Authority for Agricultural and Veterinary Chemicals 1997, *Ag Labelling Code—Code of Practice for Labelling Agricultural Chemical Products*, NRA, Canberra.