DIAFENTHIURON

National Registration Authority
For Agricultural & Veterinary Chemicals

PUBLIC RELEASE SUMMARY

of the evaluation by the NRA of the new active constituent:

Diafenthiuron

in the product:

PEGASUS MITICIDE

1996

This document is published by the National Registration Authority for Agricultural and Veterinary Chemicals. For further information, please contact -

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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 product prior to 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 & Non-Prescription Drug Branch), 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 Product" 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. More detailed technical assessment reports on occupational health and safety aspects, environmental impact, and residues in food are available from the NRA on request.

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

ABBREVIATIONS AND ACRONYMS WHICH MAY APPEAR IN THIS DOCUMENT

Diafenthiuron	Active constituent
ADI	Acceptable Daily Intake (for humans)
AHMAC	Australian Health Ministers Advisory Council
ai	Active ingredient
CNPDB	Chemicals & Non-Prescription Drug Branch (Department of Health and Family Services)
d	Day
DT50	Time period required to achieve 50% degradation in the environment
EC50	Concentration at which 50% of the test population are immobilised
EEC	Estimated Environmental Concentration
EUP	End Use Product
F_o	Original Parent Generation
h	Hour
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
Koc	Soil-water Partition Co-efficient
L	Litre
LC50	Concentration that kills 50% of the test population of organisms
LD50	Dosage of chemical that kills 50% of the test population of organisms
mg	Milligram
mL	Millilitre
MRL	Maximum Residue Limit (a legal 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 product that contain two or more poisons
TGAC	Technical Grade Active Constituent
WDG	Water Dispersible Granule
WHP	Withholding Period
WSA	Worksafe Australia

1. EXECUTIVE SUMMARY

INTRODUCTION

The National Registration Authority for Agricultural and Veterinary Chemicals (NRA) has before it an application for registration of the product PEGASUS MITICIDE and now invites comment from any person on whether this product should be registered. This invitation is being made as the active constituent contained in PEGASUS MITICIDE (*Diafenthiuron*) is new to agriculture in Australia.

The purpose of this document is to provide a summary of the data evaluated and of the regulatory considerations reached, during the evaluation by the NRA of PEGASUS MITICIDE for the control of Two Spotted Mite (*Tetranychus urticae*) in cotton.

Having completed its evaluation of the proposed use of *Diafenthiuron* in PEGASUS MITICIDE, the NRA provides the following description of that evaluation for public comment:

AGRICULTURAL ASPECTS

PEGASUS MITICIDE contains the active constituent Diafenthiuron in a suspension concentrate formulation. Diafenthiuron is in a new class of pesticides and has a novel mode of action.

Results of trials conducted in Australia have shown that PEGASUS MITICIDE, applied aerially or by ground equipment, gives effective control of Two Spotted Mite in cotton with residual activity at least as long as products containing the current industry standards Propargite and Profenofos. No phytotoxicity due to the application of PEGASUS MITICIDE was evident in any of the trials.

PEGASUS MITICIDE will fill the need for another miticide that can be used at any time through the season to provide an alternative to these standards in order to reduce resistance selection pressure on them

Registration is supported by Australian agricultural authorities.

ENVIRONMENTAL ASPECTS

Environmental Aspects

Environmental exposure to Diafenthiuron will principally involve the soil, as water solubility and vapour pressure are low. Drift to water bodies may occur from aerial application. Laboratory and field studies indicate that Diafenthiuron and its active metabolite (the carbodiimide derivative) degrade readily in soil and water. Accumulation and leaching in soils are unlikely. Bioaccumulatio of Diafenthiuron and/or its metabolites is possible due to its significant bioaccumulation factor of ~800. However, this was not demonstrated in the pond mesocosm study, indicating that

bioaccumulation is unlikely to occur in natural environments because of limited persistence and strong sorption.

Diafenthiuron is slightly to practically non-toxic to birds, soil micro-organisms and earthworms, and slightly toxic to mammals. It is highly toxic to bees and was shown to be harmful to the parasitic wasp *Apanteles plutellae*. Acute toxicity results indicate that Diafenthiuron and its carbodiimide derivative are very highly toxic to fish and aquatic invertebrates and slightly toxic to algae. Diafenthiuron's urea derivative is slightly toxic to fish and is practically non-toxic to crustaceans and algae.

Diafenthiuron shares with other miticides/insecticides already in use on cotton fields a very high toxicity to aquatic organisms. However, a significant difference is Diafenthiuron's very low persistence in the field (DT50 < 22 hours) significantly reduces its environmental exposure compared with other chemicals already in use on cotton fields.

PUBLIC HEALTH AND SAFETY ASPECTS

Toxicology

Diafenthiuron, the active ingredient of PEGASUS MITICIDE, has low acute oral and dermal toxicity and of moderate inhalational toxicity. It is a slight skin and eye irritant, but not a skin sensitiser. The PEGASUS MITICIDE formulation is expected to be of low acute oral, dermal and inhalational toxicity, slightly irritating to the skin and eyes, but not a skin sensitiser, according to the toxicity of Diafenthiuron and the formulation components.

Following repeated oral doses of Diafenthiuron, inflammatory changes in the lungs were found in rats and to a lesser extent in dogs. Similar inflammatory changes were also found in rats given high dermal doses of Diafenthiuron, indicating that dermal absorption occurs. Other significant toxic effects included swelling in a number of different tissues and effects indicative of irritation to the gastrointestinal tract in dogs, changes in biochemical parameters and/or organ weights suggestive of liver toxicity in mice and dogs, heart muscle fibrosis in rats and mice, retinal atrophy in mice, calcification in the kidneys and cerebral meninges of rats, and enlargement of the testes in rats and ovaries in dogs. These effects occurred following repeated exposure to Diafenthiuron at comparatively high doses.

Benign lung tumours were increased in female mice given Diafenthiuron at 6.75 mg/kg/d. However, this effect is not considered relevant to humans given that tumours of this type commonly occur in mice, and the incidence in treated animals was only slightly above the normal range in untreated animals. The doses required to produce this effect in mice greatly exceed any anticipated dietary intake associated with the use of PEGASUS MITICIDE. There was no evidence of a potential to affect reproductive parameters, cause birth defects or damage genetic material (DNA).

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 PEGASUS MITICIDE.

RESIDUES IN FOOD AND TRADE ASPECTS

Residues in Food

Residue data from Australian trials on cotton were presented along with previous submissions of about 20 reports of overseas trials determining Diafenthiuron residues in cotton seed, hulls, and leaf. Australian trials were conducted at the proposed maximum use rate and twice that rate. Overseas trials were at rates at and greater than those proposed for Australia. The results showed that the existing temporary MRL of 0.2 mg/kg for cotton seed could be confirmed but the temporary status was retained pending receipt of supporting studies on storage stability and effects of processing of treated cotton seed. The data and the proposed use pattern indicate the withholding period should be 5 weeks.

Data presented indicated that residues in cotton trash should not exceed 50 mg/kg but an animal feed commodity MRL was not established because the data presented were not sufficient to allow establishment of animal commodity MRLs. It was considered that residues problems should not arise through feeding cotton trash as a minor proportion of the diet of food animals. Animal (rat and goat) metabolism studies indicated that metabolism was rapid.

Trade

Although registered in many countries, Diafenthiuron MRLs have only been set by Switzerland for cole crops, cucumbers and tomatoes. Apart from New Zealand, the active is understood not to be registered in any of Australia's major trading partners. As there may could be finite residues in cotton seed because of admixed contaminating trash, the presence of Diafenthiuron residues has the potential to be a trade issue because of the absence of Diafenthiuron MRLs, especially in the main Australian cotton seed export markets (Japan, Korea, and Taiwan).

Feeding of livestock with cotton seed meal or cotton trash is not expected to lead to residues, provided the trash is fed as a minor part of the diet.

OCCUPATIONAL HEALTH AND SAFETY ASPECTS

Diafenthiuron and PEGASUS MITICIDE can be handled safely by workers when they are used in accordance with the control measures and restrictions indicated.

Diafenthiuron and PEGASUS MITICIDE are determined to be hazardous substances, according to the National Occupational Health and Safety Commission criteria.

PEGASUS MITICIDE will be formulated in Australia from imported Diafenthiuron. The product may be applied as a ground or aerial spray. One repeat application can be made, in keeping with resistance management guidelines.

The main acute hazards to end users are skin and eye irritation, while repeated exposure carries the risk of lung lesions, including via the skin. During routine use, end users may become contaminated on the skin with product or spray or inhale spray mist.

To avoid unnecessary skin contamination, workers involved in mixing, spraying or both, must wear cotton overalls buttoned to the neck and wrist, a washable hat and elbow-length PVC gloves. Workers are cautioned not to inhale spray mist, but the use of respiratory protection is

not necessary as inhalation is not expected to contribute significantly to overall exposure. Manual flagging is not permitted during aerial spraying of PEGASUS MITICIDE

In addition to critical comments and dilution rates specified on the label, an occupational health and safety restriction, that the product must only be marketed in 20 L containers with two wide neck openings, applies.

A re-entry statement relevant to workers entering treated crops appears on the product label. It details the separate restrictions for workers entering for short time periods within 24 hours of spraying and those, such as cotton chippers, entering for longer periods following the initial 24 hours after spraying.

Any new worker exposure studies or calculations on PEGASUS MITICIDE and/or Diafenthiuron exposure, are to be submitted to the National Registration Authority for Agricultural and Veterinary Chemicals for assessment.

2. INTRODUCTION

The purpose of this document is to provide the public with a summary of the data evaluated, and of the regulatory considerations reached, in the evaluation by the NRA of PEGASUS MITICIDE.

The use of PEGASUS MITICIDE is proposed as a control for Two Spotted Mite (*Tetranychus urticae*) in the cotton growing areas of NSW and Qld. The NRA now invites comment from any person on whether PEGASUS MITICIDE should be registered

Comments should be sent by 31 October 1996 to:

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APPLICANT

The applicant, Ciba-Geigy Australia Ltd, has applied for the registration of PEGASUS MITICIDE, which contains a new active constituent, *Diafenthiuron*.

PRODUCT DETAILS

PEGASUS MITICIDE is a suspension concentrate formulation containing 500g/L *Diafenthiuron*. The active constituent will be manufactured in Switzerland and the product formulated in Australia.

CURRENT OVERSEAS REGISTRATIONS OF *Diafenthiuron*

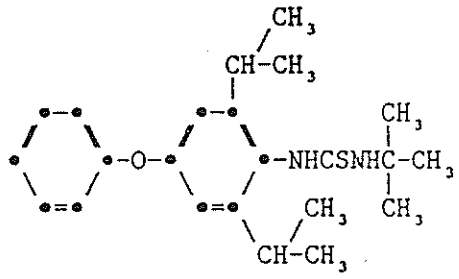
COUNTRY	CROPS
Barbados	Vegetables, Papaya
Belize	
Bielorussia	Greenhouse cucumbers and tomatoes
Brazil	
Chile	Tomatoes, cabbage, potatoes, ornamentals
China(People's Republic)	Cabbage
China (Taiwan)	Citrus
Colombia	Beans, roses
Dominican Republic	Vegetables
El Salvador	Vegetables
Egypt	Cotton
Estonia	Cucumbers, peppers, tomatoes, ornamentals
Greece	Apples, citrus, pears
Guatemala	Vegetables
Honduras	
Indonesia	Cabbage, chili peppers, potatoes
Israel	Cotton, ornamentals, vegetables
Jamaica	Vegetables
Jordan	Cucumbers, cabbage, tomatoes, ornamentals
Kazakhstan	Cotton
Latvia	Cucumbers, tomatoes
Lithuania	Strawberries
Malaysia	Vegetables, ornamentals
Mozambique	Cotton
New Zealand	Pome fruit
Nicaragua	Cotton, vegetables
Pakistan	Cotton, vegetables
Panama	Vegetables
Peru	Cotton
Romania	Tomatoes, cucumbers
Russia	Tomatoes, cucumbers
Saudi Arabia	Cucurbits, eggplant, peppers, ornamentals, potatoes
South Africa	Cotton, cucumbers
Sudan	Cotton
Switzerland	Cucurbits, eggplant, peppers, ornamentals, tomatoes, potatoes
Tanzania	Cotton, beans
Thailand	Citrus, cabbage, kale, grapes, asparagus, onions
Trinidad	Vegetables
Turkey	Cotton, watermelons, beans, eggplant
United Arab Emirates	Alfalfa, citrus, dates, mangoes, vegetables, onions
Uzbekistan	Cotton
Venezuela	Soy bean, sesame, vegetables, cotton, beans, sunflowers
Vietnam	Cabbage, cucumbers, cotton, ornamentals, tomatoes
Zimbabwe	Roses

3. PROPERTIES OF THE CHEMICAL ACTIVE CONSTITUENT

The chemical active constituent *Diafenthiuron* is manufactured in Switzerland and has the following properties:

Common name:	*Diafenthiuron*
Chemical name (IUPAC):	3-(2,6-diisopropyl-4-phenoxyphenyl)-1-tert.butyl-thiourea
Product name	PEGASUS MITICIDE
CAS Registry Number	80060-09-9
Molecular formula:	$C_{23}H_{32}N_2OS$
Molecular weight:	384.59
Appearance (colour):	white to beige
Physical state:	crystalline powder
Melting point:	149.6°C
Relative density:	1.08 g/cm^3 @ 20°C
Vapour pressure:	2.2 x 10^{-7} Pa @t 20°C
	1.6 x 10^{-6} Pa @ 30°C
	1.0 x 10^{-5} Pa @ 40°C
Water solubility (20°C):	<0.05ppm
Partition co-efficient:	$\log P_{ow} = 6.0$

Structural formula:



4. AGRICULTURAL ASSESSMENT

JUSTIFICATION FOR USE

PEGASUS MITICIDE contains the active constituent Diafenthiuron in a suspension concentrate formulation. Diafenthiuron is a new thiourea acaracide with additional insecticidal activity not previously contained in agricultural chemical product in Australia

Currently the product COMITE (Propargite) is the product of choice for the control of Two Spotted Mite. Other products used include CURACRON (Profenofos) and PREDATOR (Chlorpyrifos). PEGASUS MITICIDE, with its novel mode of action, will provide an alternative to these products in order to reduce resistance pressure on them.

Registration is supported by Australian agricultural authorities.

PROPOSED USE PATTERN

PEGASUS MITICIDE should be applied before mite damage occurs or when 30% of plant leaves are infested. Alternatively apply when 15% are infested and the rate of increase is such that 30% will be infested within 7-10 days. Only one repeat application can be made and must be within resistance management guidelines. The two applications must not be consecutive or be applied within six weeks of each other.

PEGASUS MITICIDE can be applied by ground application at 600ml/ha in a minimum of 100L water or aerially at 600-800ml/ha in a minimum of 20L of water..

EVALUATION OF EFFICACY

The applicant, Ciba-Geigy Australia Ltd, provided efficacy data to support the claims of PEGASUS MITICIDE. The reviewer of this data was satisfied that the claims for PEGASUS MITICIDE were supported by the data presented. Details of the efficacy data are:

The product has been trialed in northern NSW and Qld over the last 6 years. 17 trials involving ground and/or aerial application have confirmed that PEGASUS MITICIDE applied at 800ml/ha aerially and 600ml/ha by ground can provide effective control of mite populations that is equivalent to industry standards. Mite populations were maintained below the pre-spray levels for at least 13-21 days after application. When treatment was carried out at below threshold levels effective control was achieved for up to 38 days.

PHYTOTOXICITY

No phytotoxicity due to the application of PEGASUS MITICIDE was evident in any of the trials.

CONCLUSION

PEGASUS MITICIDE has been shown in trials to be effective for the control of Two Spotted Mite (*Tetranychus urticae*) in the cotton.

5. ENVIRONMENTAL ASSESSMENT

Environmental Fate

Diafenthiuron will be applied directly to cotton plants by aerial and ground spraying and as a consequence may also come into contact with soil and water (through spray drift and run-off). Following application, the substance is expected to partition primarily into the crop with some into the soil/sediment compartments.

- **Hydrolysis**

Hydrolysis of Diafenthiuron was investigated in aqueous media with pH values ranging from 1 to 13 and at concentrations of 1.5 ppm. The following calculated (20°C) and experimental (30°C) half-lives at environmental pH values were found:

pH	20°C	30°C
5	4.1 years	87.2 days
7	1.2 years	136.7 days
9	2.2 years	58.3 days

The results indicate that Diafenthiuron does not readily hydrolyse.

- **Photolysis**

Photolytic degradation of Diafenthiuron at a concentration of 1.5 ppm was studied in sensitised and non-sensitised solutions using an artificial light source producing a light intensity ~2.7 times higher than summer sunlight at 40° latitude. Photolysis is a major degradation mechanism for Diafenthiuron, half-life in water was 3 minutes in the sensitised solution and 38 minutes in the non-sensitised solution. The carbodiimide and urea derivatives were identified as degradation products.

No soil photolysis studies were provided, but photolysis on the soil surface is likely to be rapid based on the above study.

- **Metabolism in Soils and Aquatic Systems**

The aerobic degradation of Diafenthiuron was investigated in a range of soils (silty loams to sandy clays) at a concentration of 10 ppm. Incubation was carried out at 25°C in the dark. The aquatic metabolism of Diafenthiuron was studied under aerobic conditions at 25°C in the dark at an initial concentration of ~1 ppm. The aquatic systems consisted of natural surface water and 1% of the corresponding sediment which was used to introduce low amounts of microorganisms into the test systems.

Diafenthiuron degrades readily under aerobic soil and water conditions, half-lives of < 36 hours and ~18 days, respectively. Under aerobic soil conditions the carbodiimide derivative half-life was estimated in the order of < 10 days and urea derivative half-life was ~ 30 days.

Low levels of CO_2 were recorded in the soil and water metabolism studies, indicating slow mineralisation by soil and aquatic microorganisms. Bound residues were a major avenue for the removal of Diafenthiuron and its metabolites from the laboratory and field studies.

- **Mobility in Soil**

The adsorption of Diafenthiuron were determined by gently shaking samples (soil, active and water) in flasks, separating the phases by centrifugation and concentration of the free active determined by scintillation spectrophotometry. From these results Freundlich constants and their Koc values were determined.

Soil organic carbon partition coefficients obtained from adsorption/desorption studies on five soils indicate that Diafenthiuron is likely to strongly adsorb to soil/sediment; Koc ranged from ~2600 to 13,000.

The low mobility of Diafenthiuron was confirmed by leaching tests on packed columns of various soils (sands to silty loams). Diafenthiuron and its metabolites were not detected in the leachates or beyond a depth of 4 cm in the soil columns.

- **Field Dissipation**

Field soil and pond studies confirmed the rapid degradation of Diafenthiuron and its metabolites in the laboratory studies. Diafenthiuron degraded rapidly in the field - no parent compound was detected 2 days after application on soil, and 3 days after application in the pond only ~1% was found. The carbodiimide and urea derivatives degraded faster under field conditions, half-lives of < 2 days and ~50 days, respectively. These metabolites degraded rapidly in field pond conditions with half lives in the order of hours for the former and days for the latter, respectively.

- **Aerial application**

A field study was undertaken to monitor the distribution of aerial applied Diafenthiuron to cotton fields, near Moree, NSW. Diafenthiuron, formulated as a suspension concentrate was applied at 0.8 $L.ha^{-1}$ (400 g $ai.ha^{-1}$) in a water volume of 20 $L.ha^{-1}$. Treatments were applied using an Ayres Thrush configured with 10 Micronair AU5000 units. The nozzles were operated using a blade angle of 55 degrees. The spray was released approximately 3-4 m above the cotton canopy.

The results indicate that highest levels of drift were recovered nearest the crop. Deposit levels decayed with increasing distance from the field. Spray droplet drift extended beyond 20 m above ground level. Drift occurred up to and beyond 500 m as measured using frames covered with bridal veil. The proportion of dye recovered at 500 m relative to a vertical target placed at the field edge was 2 - 3%. At 100 m, 9% of the dye measured at the field boundary was recovered. The volume median diameter (VMD) of the droplets recorded at all distances were similar. Droplets recorded downwind from the crop had a VMD (volume mean diameter) of 50 µm.

An additional study was undertaken to determine the droplet spectra generated by a Micronair AU5000 using Pegasus. It was found that larger VMD values (71, 104 and 131 µm) were recorded at blade angles of 45°, 55° & 65° respectively. The results indicate that increasing the blade angle is likely to result in less drift due to the larger size of the droplet.

- **Accumulation and Bioaccumulation**

The rapid degradation of Diafenthiuron and its metabolites in soil indicates they are unlikely to accumulate.

Bioaccumulation of Diafenthiuron and/or its metabolites is possible due to its significant bioaccumulation factor of ~800. However, this was not demonstrated in the pond mesocosm study, indicating that bioaccumulation is unlikely to occur in natural environments because of limited persistence and strong sorption.

Environmental Effects

- **Birds**

Acute oral, dietary and reproduction tests, indicated that Diafenthiuron is slightly to practically non-toxic to the avian species tested (mallard ducks and bobwhite quails).

- **Aquatic organisms**

Acute toxicity test results for Diafenthiuron indicate very high toxicity to four species of fish (most sensitive is catfish with 96h LC50 of 1.3 ppb) and aquatic invertebrates (water flea 48h EC50 of 0.15 ppb) and slight toxicity to algae. The active carbodiimide derivative is also very highly toxic to two species of fish (rainbow trout 96h LC50 of 2 ppb) and aquatic invertebrates (water flea 48h LC50 of 0.024 ppb) and slightly toxic to algae. The urea derivative is at worst slightly toxic to fish and practically non-toxic to aquatic invertebrates and algae.

A Diafenthiuron chronic 21-day flow through study resulted in a NOEC of 0.162 ppb (highest concentration tested) for rainbow trout.

The chronic toxicity of Diafenthiuron to aquatic invertebrates (water fleas) was determined in a 21-day reproduction test. The results indicate that Diafenthiuron did not inhibit reproduction (highest concentration tested 0.09 ppb). However, the NOEC result for the total number of young of 0.001 ppb indicates that water fleas are very sensitive to Diafenthiuron.

- Pond Mesocosm study

A field pond study was conducted to determine the effects of a 500 SC Diafenthiuron formulation ai ^{14}C-labelled (acetone solvent) Diafenthiuron on the biological components of artificial ponds. To simulate spray drift the SC 500 formulation was sprayed on to the pond surfaces at the following rat 0.6 g ai.ha^{-1}, 6 g ai.ha^{-1} and 60 g ai.ha^{-1}. These rates produce an estimated initial environmental concentration in the ponds of approximately 0.1 ppb, 1 ppb and 10 ppb, respectively. In addition ru was simulated by mixing the SC 500 formulation with soil sediment which was introduced as a slurr around the edges of the ponds at a rate corresponding to 6 g ai.ha^{-1}. The ^{14}C-Diafenthiuron (60 g ai.ha^{-1}) acetone solution was also mixed in under the water surface.

Significant toxicity results only occurred at a dose of 60 g ai.ha^{-1}. The application of ^{14}C-Diafenthiuron in acetone solution (10 ppb) resulted in almost total fish mortality, whereas, the application of the SC 500 formulation (10 ppb) caused no fish mortalities. The solvent and mixing of the solution under water increase the bioavailability of Diafenthiuron relative to application as a surface spray.

Application of the SC 500 formulation resulted in daphnia population being halved after 3 to 4 hours and reduced to zero after three days, while no Daphnia could be observed in the pond that received application of the ^{14}C-labelled Diafenthiuron as an acetone solution after 3 to 4 hours. The effect on the *Daphnia* population was short-lived, as the populations recovered after 3-4 weeks. No effect on phytoplankton or pond flora was observed.

Comparison of the initial environmental concentration of Diafenthiuron in the ponds and their effects to the acute toxicity values determined in the laboratory indicates the fish results are similar and the daphnia results are an order of magnitude higher (see below).

Species	Material	Lab Results	Mesocosm Results
Bluegill sunfish	TGAC	96h LC50 = 2.4 ppb	45% mortality after 2 days at an initial EEC of 10 ppb (application by mixing under the water surface).
	EUP	No test conducted.	No mortalities recorded from the test doses at a max. EEC of 10 ppb (application by spray drift).
Daphnia magna	TGAC	48h EC50 = 0.15 ppb 48h EC100 = 0.32 ppb	100% mortality after application at an initial EEC of 10 ppb (application by mixing under the water surface).
	EUP	No test conducted.	Population halved after 3 - 4 hours at an EEC of 10 ppb (application by spray drift). Population reduced to zero after 3 days at an EEC of 10 ppb (application by spray drift).

- Field ecosystem study

The impact of Diafenthiuron on aquatic organisms was studied in a cotton growing area in Guatemala following a single application of 500 SC formulation at 500 $mL.ha^{-1}$ (250 g $ai.ha^{-1}$). Boom sprays were not turned off when passing over water bodies so as to ensure coverage of all sites.

Effect on zooplankton community was temporary as the populations recovered. The constant flow of water may carry in new specimens that populate the site again. The fish kills reported in the study were the result of direct overspray at a concentration (250 $g.ha^{-1}$) that is higher than would occur from 10% spray drift in Australia (40 $g.ha^{-1}$).

- **Non-target invertebrates**

Diafenthiuron is practically non-toxic to soil micro-organisms. Mortality endpoints indicate that Diafenthiuron can be classified as practically non-toxic to earthworms. However, the flaccidity results indicate that Diafenthiuron has sublethal effects on earthworms. Application of Diafenthiuron at a rate equivalent to 600 g ai.ha^{-1} is harmful to the parasitic wasp *Apanteles plutellae*. Diafenthiuron is highly toxic to bees.

- **Non-target plants**

No studies were provided on phytotoxicity to aquatic or terrestrial plants.

Environmental Hazard

- **Terrestrial organisms**

No wildlife hazard is anticipated from the proposed use as Diafenthiuron has low toxicity to birds and mammals. Diafenthiuron is unlikely to present a hazard to soil microorganisms and earthworms. Hazard to bees will be reduced as the draft label states, "DO NOT spray any plants in flower while bees are foraging."

- **Aquatic organisms**

- Hazard from spray drift

The aerial application study showed drift was significant. Off-target spray drift of 9% and 2 - 3% was detected at 100 m and 500 m, respectively, from the crop edge. Also, at 100 m from the crop edge the spray droplet cloud extended 20 m above ground level. The results indicate that tailwaters are likely to be contaminated with some Diafenthiuron after aerial spraying of cotton.

The extent of contamination of natural waters from drift will depend on the proximity of natural waters to cotton farms. Using the overspray figures of 2-3%[1] from the field study, a pond 15 cm deep pond, 500 m from the crop, would have an EEC of 5.4 - 9 ppb. As the EEC is greater than or equal to half the LC50 of 10 ppb, unacceptable risks can still be presumed for natural waters that occur up to 500 m from the edge of a cotton field.

The company claims that drift can be reduced by increasing the droplet size by altering the Micronair blade angle from 55^{o} to 65^{o} as recommended on the label. Increasing the blade angle has be shown to increase the droplet size (VMD) from 104 µm to 131 µm which is expected to decrease the amount of drift.

- Hazard from runoff and movement in water

The rapid degradation of Diafenthiuron and its toxic metabolite in the field and their high soil adsorptive capacity indicates contamination of natural waters from runoff is unlikely to present a hazard to the environment.

Contamination of natural waters as a result of the release of tailwaters is likely to be minimal due to the rapid degradation of Diafenthiuron in water. Diafenthiuron and its toxic metabolite have a

[1] Note this was measured 70 cm above ground and extent of deposition at this point is unclear.

DT_{50} < 22 hours and a DT90 < 3 days in the pond mesocosm study, are unlikely to persist in the aquatic environment and their environmental effects would not be chronic. The residence time in tailwaters is likely to allow "in-situ" degradation of Diafenthiuron and its active metabolite to levels where adverse environmental effects in natural waters are unlikely to occur. NSW cotton farms are known to have retention ponds and practice water recycling. Thus, off-farm movement of Diafenthiuron would be limited. Although similar water management practices do not occur in Qld cotton farms, the lengths of channels should ensure sufficient residence time to ensure levels are below toxicity when tailwaters reach natural streams.

- Hazard compared with other miticides/insecticides

Diafenthiuron shares with other chemicals already in use on cotton fields a very high toxicity to aquatic organisms. However, it is a potential improvement on existing chemical miticides and insecticides used on cotton due to its very low persistence in the environment (DT_{50} < 22 hours).

- Hazard from repeated applications

It should be noted that only one application of Diafenthiuron occurred in the aquatic mesocosm studies, whereas two applications may occur in the cotton fields. As it took the aquatic invertebrate populations 3-4 weeks to recover and the second application may occur 21 days after the first, it is not clear whether the repeat application would detrimentally affect the recovery of aquatic invertebrate populations. None of the studies provided have demonstrated that adverse effects from respray will not occur and delay recovery.

- **Desirable vegetation**

It appears from crop usage and the mode of action that deleterious effects in non-target vegetation will be unlikely to occur. No adverse effects have been observed in plant residue studies.

Conclusion

Diafenthiuron shares with other miticides/insecticides already in use on cotton fields a very high toxicity to aquatic organisms. However, a significant difference is Diafenthiuron's very low persistence in the field (DT_{50} < 22 hours) significantly reduces its environmental exposure compared with other chemicals already in use on cotton fields.

The EPA's assessment indicates contamination of the aquatic environment from runoff and discharge of tailwaters to natural waters is unlikely to present a hazard to aquatic organisms due to rapid "in-situ" degradation of these chemicals in the field and expected adsorption to soil/sediment.

Direct contamination of natural waters from drift up to a distance of 500 m from the crop edge may present a hazard to aquatic organisms. Increasing the blade angle has be shown to increase the droplet size which is expected to decrease the amount of drift. The company has amended the product label to include a recommendation that aerial application be carried out with Micronair blade angles set at 65°, thereby, reducing the hazard to aquatic organisms from spray drift.

None of the studies provided have demonstrated that adverse effects from respray will not occur and delay recovery. As it took the aquatic invertebrate populations 3-4 weeks to recover and the

initial submission indicated a second application may occur 21 days after the first, the company has proposed the following instructions regarding repeat applications:

"A repeat application can be made, if required, provided this is in keeping with resistance management guidelines. The two sprays must not be consecutive or be applied within 6 weeks of each other."

The above instructions are likely to minimise the hazard to aquatic organisms from repeat applications.

Also, the company has agreed to alert the EPA immediately of any off-target incidents associated with the use of Pegasus in cotton, such as fish kills.

6. PUBLIC HEALTH AND SAFETY ASSESSMENT

EVALUATION OF TOXICOLOGY

The toxicological database for Diafenthiuron 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

Approximately 25% of Diafenthiuron was absorbed in orally dosed rats but was quickly eliminated. Excretion mainly occurred via the bile, urine and faeces. After 7 days, only low residue levels of Diafenthiuron were found in the tissues.

Acute Toxicity

Diafenthiuron is of low acute oral toxicity in mice (LD50: 628 mg/kg/d) and rats (LD50: 2068 mg/kg/d), and of low dermal toxicity (LD50:3> 2000 mg/kg/d) and moderate inhalational toxicity (LC50: 558 mg/m) in rats. It was a slight skin and eye irritant in rabbits, but not a skin sensitiser in guinea pigs.

Based on the acute toxicity of Diafenthiuron and the concentrations of the non-active constituents of PEGASUS MITICIDE, which contains Diafenthiuron at 520 g/L, the Pegasus formulation is expected to be of low oral and dermal toxicity, of low inhalational toxicity, a slight skin and eye irritant, but not a skin sensitiser.

Short-Term Studies

Short-term (< 13 weeks) dietary administration of Diafenthiuron to rats resulted in aggregation of foam cells in the lungs, and calcification in the kidneys and cerebral meninges at 12.5 mg/kg/d, and increased mortality, reduced lymphoid cells in lungs, spleen, thymus and lymph nodes, heart muscle fibrosis, increased vacuolation in the adrenal cortex, reduced food consumption and bodyweight gains, decreased total cholesterol, and excess fluid in the chest cavity from 100 mg/kg/d.
Short-term (90 days) dietary administration of 4 mg/kg/d Diafenthiuron to dogs resulted in swelling or atrophic changes in a number of tissues, lower levels of serum protein, haemorrhage at a number of different sites, inflammation of the intestine and peritoneum, lower spleen and thymus weights, and fatty changes in renal tubules.

Short-term (28 days) dermal exposure to Diafenthiuron in rats at 150 mg/kg/d resulted in increased mortality, decreased food consumption and bodyweight gain, hunched posture, reduced movement, increased plasma proteins, slight splenic atrophy, reduced liver weights, and thoracic haemorrhage. Pulmonary toxicity was evident from 30 mg/kg/d as increased lung weights, inflammation of interstitial tissue, increased incidence of alveoli foam cells, and oedema and fibrin secretion. Slight redness occurred at the application site.

Long-Term Studies

Long-term dietary administration of Diafenthiuron to rats, mice and dogs resulted in toxic effects from approximately 3 mg/kg/d in rats and mice and 1.5 mg/kg/d in dogs. Significant effects in rats included inflammation in the lungs, and enlargement of the lungs and spleen. In mice, effects included enlargement of the liver, kidney and lung, heart muscle fibrosis, retinal atrophy, and at the highest dose level (9 mg/kg/d) the incidence of pulmonary adenoma was increased in females. However, this tumour type is known to commonly occur in the strain of mouse used in the study, and given that the incidence of this tumour only slightly exceeded that expected in female mice at the highest dose level, it is unlikely that the increased tumour incidence was related to treatment with Diafenthiuron. In dogs given Diafenthiuron at 1.5 mg/kg/d or above, effects included enlarged livers which were associated with changes in biochemical parameters suggestive of liver toxicity, effects indicative of irritation to the gastrointestinal tract, oedematous changes in the pancreas and thymus, and lower spleen and thymus weights. Enlargement of the testes in rats and ovaries in dogs were not associated with any histopathological findings. Other effects found in all species included increased mortality at the higher doses, lower food consumption and bodyweights, and non-specific changes in some haematological and biochemical parameters.

Reproduction and Developmental Studies

In rats, dietary administration of Diafenthiuron over two generations at doses up to 10.2 mg/kg/d did not affect reproductive parameters, nor the development of offspring.

There was no evidence of birth defects reported in rats and rabbits given oral doses up to 30 and 2 mg/kg/d, respectively, during the period of embryonic development.

Genotoxicity Studies

Diafenthiuron was not mutagenic in bacterial or mammalian cells in vitro, and did not induce nuclear anomalies in Chinese hamster bone marrow cells, chromosomal aberrations in human lymphocytes or unscheduled DNA synthesis in rat hepatocytes or human fibroblasts. These findings indicate that Diafenthiuron does not cause damage to DNA.

PUBLIC HEALTH STANDARDS

Poisons Scheduling

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

The NDPSC recommended that Diafenthiuron 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.

NOEL/ADI

The most sensitive species were rats and dogs with NOELs of 0.3 mg/kg/d. In order to calculate the 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 the extrapolation of 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 0.003 mg/kg/d for Diafenthiuron was established.

7. RESIDUES IN FOOD AND TRADE ASSESSMENT

Background

Diafenthiuron is a thiourea derivative with acaricidal and insecticidal activity. It is formulated in Pegasus 500 SC Miticide as a suspension concentrate containing 500 g Diafenthiuron/L. The product can be used on brassicas, green beans, potatoes, tomatoes and cotton. A temporary MRL of 0.2 mg/kg was previously established in Australia for cotton seed..

Appropriate residue and metabolism studies were provided in accordance with the *Requirements for Clearance of Agricultural and Veterinary Chemical Products,* to support the use of Diafenthiuron on cotton.

RESIDUES IN FOOD COMMODITIES - COTTON SEED

In a previous submission, approximately 20 reports of overseas trials (Greece, Israel, South Africa, Spain, Turkey and Guatemala) determining residues in cotton seed (dehulled or delinted), hulls and leaf were provided. Application rates (g ai/ha) included 1x 750, 2x 400, 3x 500, 5x 200, 7x 400 and 8x 300 with preharvest intervals from 0-51 days. The major residue in cotton seed was a metabolite and the maximum detected was 0.05 mg/kg at preharvest intervals of 7 or less days. The maximum total residue (sum of metabolites) detected was equivalent to 0.11 mg/kg in cotton seed.

Four Australian trials were described in two reports. At Warren in NSW, two treatments at 480 g ai/ha caused total equivalent residues of 0.77 mg/kg at 20 days while double treatment resulted in similar levels. However these results were probably caused by contamination after harvest. Applications of 400 or 800 g ai/ha at Moree, NSW and Melrose, QLD, all gave total residue in seed less than 0.1 mg/kg at 34 or 36 days. Summaries of trials conducted at Moree and Nevertire in NSW at rates of 400 and 800 g ai/ha with withholding periods of 36 and 39 days reported the maximum total residue (sum of metabolites) was equivalent to <0.12 mg/kg.

The data together with the use pattern indicate that the withholding period should be five weeks and that the existing temporary MRL of 0.2 mg/kg be confirmed but retained as a temporary MRL pending receipt and evaluation of supporting studies on storage stability and effects of processing. The expiry date for the cotton seed MRL has been extended to 31 December 1999.

Residues in animal feeds - cotton trash

Residues on cotton trash were related to application rate. 34-36 days after 400 g ai/ha, total equivalent residue was 22 mg/kg at Moree and 20.5 mg/kg at Melrose while after 800 g ai/ha, levels were 50.2 and 39.1 mg/kg. Metabolism data obtained dosing labelled compound to rats and goats indicated that although metabolism was rapid, label in liver was as high as 0.6 mg/kg after equivalent of 5 ppm in feed. However lambs given 20 mg/kg bw/d for 56 days had no detectable residues in tissue except up to 0.12 mg/kg in some fat samples. Data is not sufficient to set MRLs for food products of animal origin, but it is considered that residue problems should not arise through feeding cotton trash as a minor proportion of the diet to food animals. Avoidance of long term cotton trash feeding and not feeding trash for sometime before slaughter would also be expected to further reduce the risk of measurable residues being present in animal commodities.

Plant Metabolism

The major metabolites of Diafenthiuron are N[2,6-bis(1-methylethyl)-4-phenoxy-phenyl]-N'-(1,1-dimethylethyl)carbodiimide (CGA 140408) and N[2,6-bis(1-methylethyl)-4-phenoxy-phenyl]-N'-(1,1-dimethylethyl)urea (CGA 177960).

Cotton plants were treated with ^{14}C-labelled Diafenthiuron. There was limited penetration of ^{14}C in to leaf and half-life of the parent compound on the leaf surface was about 60 hours. Residues in bolls were believed to occur because of volatility. No parent compound was detected but ^{14}C equivalents (mg/kg) were 0.040 in fibre, 0.042 in seed and 0.141 in hulls.

Tomato plants were treated with ^{14}C-labelled Diafenthiuron at 30 g ai/ha. There was limited penetration of ^{14}C in to leaf and half-life of the parent on the surface was about 48 hours. Degradation proceeded photolytically to CGA 140408 and then on to CGA 177960 which was the major metabolite detected. At harvest total residue was 1 mg/kg in foliage but only 0.02 mg/kg was parent compound. In tomatoes residue of parent was 0.001 mg/kg.

Rotational crops of lettuce, carrots wheat and corn were grown in soil which was treated with 0.32 kg Diafenthiuron/ha. This was estimated to be equivalent to run-off from three treatments at 400 g ai/ha. Most of ^{14}C remained in the 0-5 cm layer and the major component of the soil residue was CGA 177960. There was some take-up of residue with the highest equivalent residue being in mature wheat stalks at 0.11 mg/kg but this was not considered of significance.

Animal metabolism

In rats orally dosed once with Diafenthiuron labelled with ^{14}C in the isopropyl group at 0.5 or 50 mg/kg bw, excretion was rapid via faeces with a small proportion of very polar metabolites in urine. Only 1-4% of the Diafenthiuron was detected unchanged in faeces. The major metabolite was CGA 177960 and this was produced both after absorption and within the intestine. Residues of ^{14}C in tissues 7 days after 0.5 mg/kg were less than 0.02 mg/kg except liver and heart at 0.04-0.05 mg/kg. Half lives for depletion of ^{14}C ranged from 2-3 days for fat and blood to 12-17 days for brain and heart. Following the low dose, label in all tissues had dropped below 0.1 mg/kg in 72 hours. After 50 mg/kg, label residues were high - at 14 days label equivalent to 1.3 mg/kg was detected in liver, and smaller amounts in other tissues.

In **goats** dosed at equivalent to 5 ppm in diet for four days metabolism appeared to be similar to that in the rat. Initial product appears to be the reactive CGA 140408 which is converted to CGA 177960 and then conjugated with fatty acids. Several minor metabolites were also detected but no parent compound was present. Maximum equivalent residue in milk was 0.029 mg/L and highest tissue residue was in liver at 0.6 mg/kg, nine hours after final dose. The urea metabolite, CGA 177960, was the major metabolite identified. This metabolite was present in fat at a concentration of 0.04 ppm (29% of the tissue residue) and in liver at 0.014 ppm (2.4% of the tissue residue).

Animal transfer study

Diafenthiuron was given orally to lambs at 20 mg/kg bw/d for 56 days and animals sacrificed at intervals during dosing and at 14 days after final dose, and blood and tissues taken for analysis for the most common metabolite CGA 177960. CGA 177960 was not detected in blood or plasma (<0.01 mg/L) nor in was it detected in muscle, liver, kidney or subcutaneous fat (<0.02 mg/kg). Residues were detected in omental and renal fat with the maximum level at 56 days (0.12 mg/kg). 14 days after final dose the only residue detected was in renal fat at 0.02 and 0.05 mg/kg

Analytical methods

Detailed descriptions of analytical methods were provided for Diafenthiuron and its two major metabolites CGA 140408 and CGA 177960.

Diafenthiuron and CGA 140408 were extracted, cleaned up on QMA Sep-Pak Plus and determined by reverse phase HPLC using UV detection at 256 nm.

CGA 177960 was extracted, cleaned up first on a QMA Sep-Pak Plus and then on a silica Sep-Pak, and quantitated by reverse phase HPLC with UV detection at 230 nm. In animal tissues, fat, blood and plasma was extracted and cleaned-up in a similar manner but was quantitated by normal phase HPLC with UV detection at 230 nm.

Residue definition

The definition previously proposed and accepted by the applicant was:

> Sum of Diafenthiuron; N-[2,6-bis(1-methylethyl)-4-phenoxy-phenyl]-N'-(1,1-dimethylethyl)urea; and N-[2,6-bis(1-methylethyl)-4-phenoxy-phenyl]-N'-(1,1-dimethylethyl)carbodiimide, expressed as Diafenthiuron.

This definition is appropriate and its continued use is supported.

Storage stability studies

Storage stability studies in cotton seed, cotton seed by-products, and animal tissues were not presented and the applicant has been requested to supply appropriate studies to show that residues are stable under expected sample storage conditions. Argument that stability of residues in faeces indicated stability in animal tissues was not relevant enough to show stability of residues in animal tissues.

Processing study

An Australian processing study on cotton seed treated at 400 and 800 g Diafenthiuron/ha was conducted in which the cotton seed was processed into oil and various fractions. Initial residues in the seeds were 0.04 mg/kg Diafenthiuron, <0.02 mg/kg of CGA 140408, and 0.04 or 0.08 mg/kg of CGA 177960. Hulls, meals and oils contained no detectable residues (<0.02 mg./kg) of Diafenthiuron or its metabolites. The study was considered to have probably supported the claim that Diafenthiuron and its by-products do not accumulate in cotton seed by-products but not to have proven it as the original residue levels in the cotton seed were too low to be certain what happened to them during processing. The applicant has been asked to address this further.

MRL Standard

No changes to the current MRL Standard Table 1 and Table 3 entries for Diafenthiuron are required with respect to the cotton seed entry and residue definition. The present expiry date has been extended to 31 December 1999.

Withholding period

The withholding period following use on cotton should be five weeks:

DO NOT HARVEST FOR FIVE WEEKS AFTER APPLICATION

TRADE CONSIDERATIONS

Diafenthiuron uses on various vegetables, fruits and cotton are registered overseas but only Switzerland has established MRLs (for vegetable crops). No registrations appear to have been issued in other Western European countries or the United States of America. The Codex Alimentarius Commission has not established Diafenthiuron MRLs.

The main export markets for Australian cotton seed were stated to be Japan, Korea, and Taiwan. Exporters of cotton seed need to recognise there is a possibility of measurable Diafenthiuron residues in the seed especially if contaminating cotton trash is present.

Overseas data on residue levels in cotton seed hulls and the Australian cotton processing data indicated that hulls, meal, and oil are expected to contain no or low levels of Diafenthiuron and its metabolites and animal consumption of cotton seed by-products such as meal or hulls would not be expected to lead to animal commodity residues. Although there can be high levels of Diafenthiuron in cotton trash, feeding of such trash to animals as either a minor proportion of the diet or intermittently is also expected to result in minimal residues in animal commodities especially if feeding of the trash stops some time before slaughter to allow any residues to deplete to non-measurable levels.

8. OCCUPATIONAL HEALTH AND SAFETY ASSESSMENT

Introduction

Diafenthiuron is determined to be a hazardous substance by Ciba-Geigy Australia Ltd, according to the National Health and Safety Commission (NOHSC) Approved Criteria for Classifying Hazardous Substances. The health effects relevant to the classification are acute oral toxicity, acute inhalation toxicity and the development of lung lesions following repeated exposure via the oral and dermal routes. Substances containing Diafenthiuron are hazardous when it is present in concentrations equal to or above 3%.

The technical grade active constituent will be imported in steel drums containing 45 kg of the chemical.

Diafenthiuron is a white to beige odourless crystalline powder with low vapour pressure. It is Class 6.1 dangerous goods, under the Australian Code for the Transport of Dangerous Goods by Road and Rail (ADG Code).

The end use product, PEGASUS MITICIDE, is also determined to be a hazardous substance, according to NOHSC criteria.

PEGASUS MITICIDE is an odourless light to dark grey fluid paste. It will be formulated in Australia from imported active ingredient and packed in 20 L drums with two wide neck openings. The product is not classed as dangerous goods, under the ADG Code.

Formulation, transport, storage and retailing

Chemical industry workers involved in the formulation, testing and packaging of the product should be protected by an air extraction system and safe work practices and receive training commensurate with the risks identified in the workplace assessment process. These workers should wear gloves, overalls, safety boots, respirator and eye protection.

Workers involved in the transport, storage and retailing of Diafenthiuron or the end use product could only be contaminated if the packaging were breached.

Advice on the safe handling of Diafenthiuron and PEGASUS MITICIDE during routine transport, storage and retailing, is provided on the respective labels and material safety data sheets (MSDS). The labels and MSDS contain adequate information to enable workers to handle spills.

End use

PEGASUS MITICIDE is diluted with water and applied to cotton as a ground or aerial spray. Product application rates per hectare are 600 mL for ground application and 600-800 mL for aerial application, in minimum volumes of 100 L and 20 L respectively. The maximum concentration of the product in the ground spray is 0.6% (0.3% Diafenthiuron) and 3%-4% (1.5% - 2% Diafenthiuron) in the aerial spray.

The main acute hazards to end users are skin and eye irritation. Repeated exposure via the oral and dermal routes carries the risk of lung lesions.

End users may become contaminated with PEGASUS MITICIDE during routine use. The main route of occupational exposure to the product and spray is by skin contamination. Inhalation of spray mist is also possible.

Worker exposure and risk when handling PEGASUS MITICIDE for ground spraying was estimated using the Predictive Operator Exposure Model. Exposure and risk when mixing/loading for aerial spraying was estimated using surrogate data from a field exposure study on cotton using a different chemical. The risk assessment indicated that as well as the normal requirement for personal protective equipment within the product safety directions, additional restrictions were necessary to safeguard all workers using PEGASUS MITICIDE.

In the product safety directions, workers are warned to avoid skin and eye contact with the product and not to inhale spray mist. End users handling concentrated PEGASUS MITICIDE and carrying out spraying operations should wear cotton overalls buttoned to the neck and wrist, a washable hat and elbow-length PVC gloves. Workers are not required to use respiratory protection, as inhalation is not expected to contribute significantly to overall exposure.

Additional restrictions for PEGASUS MITICIDE apply to container dimensions, application frequency and manual flagging. These are detailed below.

Entry into treated areas or handling treated crops

Workers re-entering treated areas may become contaminated from residues on the crop foliage. Repeated dermal exposure carries the risk of adverse health effects. Accordingly, re-entry restrictions are required for workers entering for short periods of time within 24 hours of spray application and cotton chippers. Both these groups of workers require overalls and gloves. The product label contains a re-entry restriction relevant to both these worker groups.

Considering the five week withholding period and that cotton harvesting and subsequent handling will be mechanical operations, worker exposure during harvesting or re-handling is not of occupational health and safety concern.

Recommendations for safe use - all workers

- Formulation and packaging

Workers involved in the formulation, testing and packaging of the product should be protected by an air extraction system with adequate ventilation, adopt safe work practices and receive appropriate training.

Where product manufacturing processes are not fully contained, workers should wear gloves, overalls, safety boots, respirator and eye protection.

- Package dimensions

PEGASUS MITICIDE must only be packaged in 20L containers with two wide neck openings.

- End use

End users should follow the instructions and safety directions on the product label. They should wear cotton overalls buttoned to the neck and wrist, a washable hat and elbow-length PVC gloves, when opening containers, preparing spray and using the prepared spray.

The product must be used only at 600 mL product per hectare as a ground spray and 600-800 mL product per hectare as an aerial spray. The product should be diluted in a minimum of 100 L of water/ha for ground application and a minimum of 20 L of water/ha for aerial application. Only one repeat application is permitted. The two sprays must not be applied within 6 weeks of each other.

Manual flagging is not permitted during the aerial application of PEGASUS MITICIDE.

- Personal protective equipment

Personal protective equipment worn by all workers should conform with the relevant Australian standard as follows:

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

Overalls - AS 3765-1990, Clothing for Protection Against Hazardous Chemicals

Safety boots - AS/NZS 2210 - 1994, Occupational Protective Footwear

Respirator - AS/NZS 1715-1994, Selection, Use and Maintenance of Respiratory Protective Devices and AS/NZS 1716-1994, Respiratory Protective Devices

Eye protection - AS/NZS 1337 - 1992, Eye Protectors for Industrial Applications

- Re-entry statements

The following re-entry statement must be included on the product label:

Re-entry period

"Do not allow entry into treated areas for 24 hours after treatment. If exceptional circumstances require prior entry, limit duration of entry and wear cotton overalls buttoned to the neck and wrists and elbow-length PVC gloves. Clothing must be laundered after each day's use."

Cotton chippers:

"Do not allow entry into treated areas for 24 hours after treatment. When entering treated areas between 24-72 hours after treatment, wear cotton overalls buttoned to the neck and wrists (or equivalent clothing) and gloves. Clothing must be laundered after each day's use."

- Active constituent label

Diafenthiuron should be labelled in accordance with NOHSC National Code of Practice for the Labelling of Workplace Substances.

- MSDS

Manufacturers and importers should produce a MSDS for Diafenthiuron and PEGASUS MITICIDE. These should contain information relevant to Australian workers, as outlined in 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.

- Further information required

Exposure data - Any new worker exposure studies (including re-entry studies), dislodgeable foliar residue data or calculations on PEGASUS MITICIDE and/or Diafenthiuron exposure, must be submitted to the National Registration Authority for Agricultural and Veterinary Chemicals (NRA), to be forwarded to Worksafe Australia for assessment.

Conclusions

Diafenthiuron can be used safely by formulation workers if handled in accordance with the instructions on the active constituent label and MSDS.

PEGASUS MITICIDE can be used safely on cotton, if handled in accordance with the instructions on the label and the restrictions specified in this report. Additional information is available in the product MSDS.

ANNEX 1

CAUTION

KEEP OUT OF REACH OF CHILDREN

READ SAFETY DIRECTIONS BEFORE OPENING OR USING

PEGASUS ®

MITICIDE

Active Constituent: 500 g/L diafenthiuron

Controls Two Spotted Mite in Cotton

20 Litres

Ciba-Geigy Australia Limited, 140 - 150 Bungaree Road, Pendle Hill, NSW 2145 N1 UN-No. free

Directions for Use:

Crop	Pest	State	Rate/ha	Critical comments
Cotton	Two spotted mite (*Tetranychus urticae*)	NSW & Qld only	600 mL - 800 mL.	Apply before mite damage occurs or when 30% of plant leaves are infested. Alternatively apply when 15% of plants are infested and the rate of increase is such that 30% of plants are likely to be infested within 7-10 days. A repeat application can be made, if required provided this is in keeping with resistance management guidelines. The two sprays must not be consecutive or be applied within 6 weeks of each other. Only use the lower rate when application is by ground based equipment. Thorough spray coverage is essential. Ground application should involve the use of droppers with nozzles pointing upwards to ensure adequate deposits on the underside of leaves. Apply Pegasus miticide under a pest management program that includes regular crop checking.

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

TO AVOID UNACCEPTABLE RESIDUES:
DO NOT FEED ANY PORTION OF THE PLANTS TO LIVESTOCK OR POULTRY FOR 5 WEEKS AFTER APPLICATION.
DO NOT PROCESS INTO FOOD FOR 5 WEEKS AFTER APPLICATION.

General Instructions

Start treatment at the beginning of a mite infestation ie. where mite infestation levels do not exceed 30% or where regular counts indicate an increase in the percentage of leaves infested on consecutive checks. Treatment at higher infestation levels may lead to unsatisfactory results. When sampling for mites follow the current CSIRO presence or absence sampling method.

Mixing

Add required amount of Pegasus miticide to clean water in half filled spray tank with the agitator or by-pass in operation. Maintain agitation while filling tank with remainder of water. Agitation must also be maintained throughout the spray operation.

Application

To be effective Pegasus miticide requires thorough spray coverage. Ensure that equipment is properly calibrated to give an even distribution at the correct volume.
Ground application: Apply as a spray in a minimum of 100 L of water/ha. The use of hollow cone nozzles and droppers are recommended.
Aerial application: Apply in a minimum of 20 L of water/ha, to assure thorough coverage of the crop. Where Micronair rotary atomisers are used blade angles of 65° should be used. Pegasus miticide should not be applied when wind speeds are below 1 m/s or exceed 4 m/s. Application of Pegasus miticide should be avoided when temperatures exceed 28° - 30° C. Manual flagging is not permitted during aerial spraying of Pegasus Miticide.

Compatibility
Pegasus miticide is compatible with Larvin† 375 SC, Decis† 25 EC, Endosulfan† 350 EC and *Bacillus thuringiensis* biological insecticides.

Protection of Livestock
Dangerous to bees. DO NOT spray any plants in flower while bees are foraging.

Protection of Wildlife, Fish, Crustaceans and Environment
Very dangerous to fish and crustaceans. DO NOT contaminate streams, rivers or waterways with the chemical or used container. For aerial application do not apply under meteorological conditions where spray may drift onto adjacent water bodies. When passing over water bodies ensure boom spray is turned off.

Storage and Disposal
Store in the closed, original container in a dry, well ventilated area as cool as possible out of direct sunlight.

Triple or (preferably) pressure rinse containers before disposal. Add rinsings to the spray tank. DO NOT dispose of undiluted chemicals on-site. Break, crush, puncture or bury empty containers in a local authority landfill. If not available, bury the containers below 500mm 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.

Empty container are recyclable and can be returned to any one of Ciba's distributors.

Re-Entry Period
DO NOT allow entry into treated areas for 24 hours after treatment. If exceptional circumstances require prior entry, limit duration of entry and wear cotton overalls buttoned to the neck and wrists, and elbow-length PVC gloves. Clothing must be laundered after each day's use.

Cotton chippers - DO NOT allow entry into treated areas for 24 hours after treatment. When entering treated areas between 24-72 hours after treatment, wear cotton overalls buttoned to the neck and wrists (or equivalent clothing) and gloves. Clothing must be laundered after each day's use.

Material Safety Data Sheet
If additional hazard information is required refer to the Material Safety Data Sheet. For a copy telephone 1800 025 931.

SAFETY DIRECTIONS
Will irritate the eyes and skin. Avoid contact with eyes and skin. DO NOT inhale spray mist. When opening the container, preparing the spray and using the prepared spray wear cotton overalls buttoned to the neck and wrist (or equivalent clothing) and washable hat, elbow length PVC gloves and impervious footwear.

If product gets on skin, immediately wash area with soap and water. After use and before eating, drinking or smoking, wash hands, arms and face thoroughly with soap and water. After each days use, wash gloves and contaminated clothing.

FIRST AID
If poisoning occurs contact a doctor or Poisons Information Centre. If swallowed and if more than 15 minutes from a hospital induce vomiting, preferably using Ipecac Syrup (APF).

MANUFACTURER'S WARRANTY AND EXCLUSION OF LIABILITY
This product as supplied is of a high grade and believed to be suitable for any purpose for which it is expressly recommended and must be used in accordance with the direction for use given on the label. No responsibility is accepted in respect of this product, save those non-excludable conditions implied by any Federal and State Legislation or law of a Territory.

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