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Public Release Summary
on

Evaluation of the new active

CARBOSULFAN

in the product

MARSHAL® 250 EC INSECTICIDE

National Registration Authority
for Agricultural and Veterinary Chemicals

Canberra
Australia

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[redacted]

[redacted]

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 health.

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 *Interim Requirements for the Registration of Agricultural and Veterinary Chemical Products*.

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.

Contents

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
F_O	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 for registration of the product Marshal® 250 EC Insecticide 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 Marshal® 250 EC Insecticide, Carbosulfan, 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 of Marshal® 250 EC Insecticide for use as a soil applied treatment at planting in cotton.

Having completed its evaluation of the proposed use of Carbosulfan in Marshal® 250 EC Insecticide, the NRA provides the following description of that evaluation for public comment.

AGRICULTURAL ASPECTS

Marshal® 250 EC Insecticide contains the active constituent Carbosulfan in an emulsifiable concentrate formulation containing 250 g/L Carbosulfan.

It is proposed to use this product to protect emerging and young cotton against thrips, jassids, wireworms, leafhoppers and green mirids. Results of trials conducted in Australia have shown that Carbosulfan can provide early season control of these potentially yield-reducing pests and is less toxic than products of equal efficacy currently registered.

Registration is supported by Australian agricultural authorities.

ENVIRONMENTAL ASPECTS

Carbosulfan rapidly degrades to Carbofuran, with half-lives of <1 day by hydrolysis, at neutral and acid conditions, and <5 days in soil under both aerobic and anaerobic conditions. The hydrolysis half-life is 7 days under basic conditions, pH 9. Carbofuran is much more stable particularly under anaerobic conditions.

The mobility of Carbosulfan was found to be low, with K_{oc} between 1660 and 2600. The major metabolite, Carbofuran, is a known leacher. However, in a two-year lysimeter study it was shown that Carbosulfan and Carbofuran did not leach below 40 cm and that significant degradation had occurred. Carbosulfan is not expected to bioaccumulate due to its rapid degradation. However, depuration of radiolabel in one test was incomplete after 30 days.

From tests provided, Carbosulfan can be regarded as highly to very highly toxic to birds, fish and *Daphnia*. Aquatic toxicity tests were limited, as only two fish species and *Daphnia* had been tested for acute toxicity. No 21-day *Daphnia* tests were available, and the range of aquatic species was limited.

Carbosulfan is highly toxic to birds, bees, fish and aquatic invertebrates. However, the method of application should be such that exposure, and therefore hazard, to these animals is limited. Nonetheless, Environment Australia is seeking monitoring data from the company during the first year of use to confirm this prediction.

PUBLIC HEALTH AND SAFETY ASPECTS

Toxicology

Carbosulfan, the active ingredient in Marshal® 250 EC Insecticide, has moderate to high oral toxicity, low skin toxicity and moderate inhalational toxicity. It is a slight skin and eye irritant, and causes skin sensitisation. The formulated product has moderate to high oral toxicity, moderate skin and inhalational toxicity, is a moderate skin and eye irritant and causes skin sensitisation.

Long-term administration of Carbosulfan to mice, rats and dogs at high doses caused reduced body weights and cholinesterase inhibition. Spleen weights were reduced at high doses in mice and dogs and brain weights were increased in mice. Urinary alterations, red blood cell and white blood cell variations were noted in rats at high doses.

Three generations of rats exposed to Carbosulfan exhibited lower birth weights, reduced litter size and reduced survivability at a dose which caused toxicity to adult animals. Carbosulfan did not affect the foetal development of rabbits. In rats, doses which were toxic to adult animals caused lower foetal weights and retarded bone formation of the sternebrae. There was no evidence that Carbosulfan causes damage to genetic material.

Conclusion

Based on an assessment of the toxicology and the fact that there should be minimal dietary intake of residues, no adverse effects on human health are considered likely from the proper use of this product.

RESIDUES IN FOOD AND TRADE ASPECTS

Residues in food

Carbosulfan is a carbamate insecticide which, when applied to the soil, readily converts to the already registered insecticide, Carbofuran. Results from cotton residue trials conducted in Australia showed that residues of Carbosulfan and of Carbofuran in harvested cotton seed and fodder (arising from the soil application of Marshal® 250 EC at the time of sowing the cotton seed) met the current Carbofuran Maximum Residue Limits (MRLs) of *0.05 mg/kg and 2 mg/kg for cotton seed and primary feed commodities respectively.

A harvest withholding period is not required by the proposed use pattern as residues at harvest are expected to be non-quantifiable. Residue data from an overseas cotton trial supported these MRLs.

Carbosulfan and Carbofuran residues in animal commodities (as a result of eating feed made from cotton by-products obtained from treated cotton seed) are not expected to exceed the current Carbofuran animal commodity MRLs of *0.05 mg/kg for meat [mammalian], and *0.05 mg/kg for (milks) when Marshal® 250 EC Insecticide is used according to the proposed use pattern.

Trade

Exported cotton, cotton seed and cotton fodder are not expected to have measurable residues of Carbosulfan and to have Carbofuran at concentrations no greater than 0.05 mg/kg. Provided these values comply with the requirements of importing countries, such residues should be of little consequence. Feeding of stock with cotton seed meal or fodder obtained from Carbosulfan treated crops using the proposed use pattern is considered unlikely to result in residues in the animals.

OCCUPATIONAL HEALTH AND SAFETY ASPECTS

Marshal® 250 EC Insecticide can be safely used by workers when handled in accordance with the control measures indicated in this assessment.

Carbosulfan and Marshal® 250 EC Insecticide are determined to be hazardous substances according to NOHSC criteria. Hazardous substances are subject to the workplace controls outlined in NOHSC (1994c).

Marshal® 250 EC Insecticide will be formulated in Australia. Closed systems will be used during mixing operations. Drum decanting and filling operations will be conducted under local ventilation. Workers at the formulation plant will be required to wear appropriate personal protective equipment.

Marshal® 250 EC Insecticide will be applied at seed planting only. It will be sprayed directly into the planting furrow over cotton seed and covered immediately by soil. During product use, worker's skin may become contaminated when mixing and loading product, applying spray and cleaning up spills and equipment. The main hazards associated with the product are skin and eye irritation, skin sensitisation and cholinesterase inhibition. The risk assessment indicates that adequate worker controls can be instituted to enable safe use of the product.

During spray preparation, workers should wear cotton overalls buttoned to the neck and wrist and a washable hat, elbow-length PVC gloves and face shield or goggles. During spray application workers should wear cotton overalls buttoned to the neck and wrist and a washable hat and elbow-length PVC gloves.

Re-entry workers do not require protective equipment.

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 Marshal® 250 EC Insecticide.

Applicant

The applicant, FMC International A.G., has applied for the registration of Marshal® 250 EC Insecticide, which contains a new active constituent, Carbosulfan.

Product and use details

Marshal® 250 EC Insecticide is an emulsifiable concentrate formulation containing 250 g/L Carbosulfan. The product will be formulated and packaged in Australia.

The use of Marshal® 250 EC Insecticide is proposed as an early season control for thrips, jassids, wireworms, leafhoppers and green mirids all areas of Australia where cotton is grown. Carbosulfan has a broad spectrum of activity. It has been shown to be more effective and is less toxic than the currently accepted industry standards, Aldicarb and Phorate. The NRA now invites comment from any person on whether Marshal® 250 EC Insecticide should be registered

Comments should be sent by 12 October 1997 to:

[redacted]

[redacted]

Current overseas registrations of Carbosulfan

Carbosulfan is registered for use on cotton in the following countries:

Brazil	Greece	Pakistan
China	India	Paraguay
Colombia	Israel	Spain
Costa Rica	Ivory Coast	Thailand
Dominican Republic	Kenya	Turkey
Egypt	Mozambique	
Ecuador	Nicaragua	
El Salvador	Republic of South Africa	

Gazette Granule and Advantage Granule (Carbosulfan) are registered in Japan for a number of uses including rice, sugarcane, melons, watermelons, eggplant, wax gourd, radish, cabbage, onion, broccoli, sweet potato, strawberries and tobacco.

In South Korea, Marshal 3G is used in rice.

The use patterns are similar as the product is applied at or soon after planting. The use rates are generally higher than those proposed for use in Australia.

Chemistry and Manufacture

Active constituent

The chemical active constituent Carbosulfan is manufactured in USA and has the following properties:

Common name (ISO): Carbosulfan

Chemical name: 2,3-dihydro-2,2-dimethyl-7-benzofuranyl(dibutylaminothio) methylcarbamate (IUPAC)

Product name: MARSHAL® 250 EC INSECTICIDE

CAS Number: 55285-14-8

Empirical formula: $C_{20}H_{32}N_2O_3S$

Molecular weight: 380.5

Physical form: Viscous liquid

Colour: Orange to brown clear

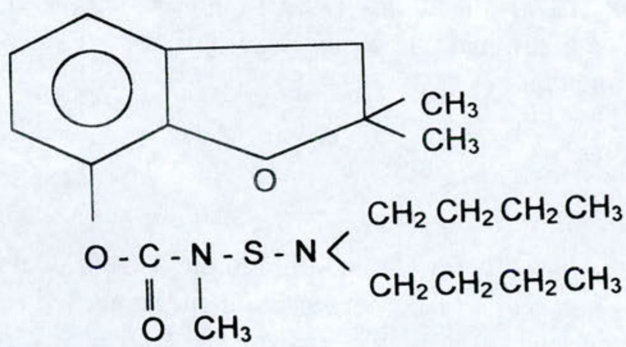
Odour: Mildly phenolic

Density: 1.056 g/ml

Octanol/water partition coefficient (K_{OW}): 2068+/-641

Vapour pressure: 0.31 X 10^{-6} at 25°C:

Structural formula:



Toxicological Assessment

The toxicological database for Carbosulfan 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 increased the likelihood that potentially significant 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 vitro studies have revealed that in acidic conditions, such as in the stomach, Carbosulfan rapidly cleaves to produce Carbofuran. In rats, Carbosulfan was rapidly metabolised and eliminated via the urine, faeces and breath. The main excretory organ was the kidney.

Acute studies

Carbosulfan was of moderate to high oral toxicity (LD_{50}= 32.7 mg/kg bw in mice, 185 mg/kg bw in rats). Carbosulfan was of low dermal toxicity (LD_{50} >2000 mg/kg bw in rabbits). Rats which inhaled Carbosulfan displayed moderate toxicity (LC_{50}= 610 mg/m^3). Toxic signs at high doses in these species included tremors, salivation and excessive tears. Carbosulfan is a slight eye and skin irritant in rabbits and caused skin sensitisation in guinea pigs.

The product, Marshal® 250 EC Insecticide, caused moderate acute oral (LD_{50}= 87.5 mg/kg bw in male rats), dermal (LD_{50}= 1520 mg/kg bw in male rabbits) and inhalational (LC_{50}= 1060 mg/m^3) toxicity. The product was a moderate skin and eye irritant to rabbits and caused skin sensitisation in guinea pigs.

Subchronic studies

Rats were fed up to 50 mg/kg bw/day Carbosulfan in the diet for 90 days. Cholinesterase levels in erythrocytes, plasma and brain were significantly inhibited at 50 mg/kg bw/day. At this dose lower specific gravity of urine was noted. The NOEL was 2 mg/kg bw/day.

Dogs were fed up to 35 mg/kg bw/day Carbosulfan in the diet for six months. Decreased body weights were noted in dogs fed 35 mg/kg bw/day Carbosulfan. Plasma cholinesterase levels were inhibited at 16 mg/kg bw/day and above but, levels of cholinesterase in red blood cells were inhibited at 35 mg/kg bw/day only. Serum protein levels were decreased in 35 mg/kg bw/day dogs and spleen weights were reduced at 16 mg/kg bw/day males and over. The NOEL was 2 mg/kg bw/day.

Long-term studies

Mice were fed up to 320 mg/kg bw/day Carbosulfan in the diet for 24 months. At the highest dose, adverse ocular effects and lower body weights were noted. Cholinesterase inhibition was found in the plasma, red blood cells and brain and spleen weights were reduced at doses of 62 mg/kg bw/day and above. The NOEL was 1.3 mg/kg bw/day. Tumours were not increased.

Rats were fed up to 213 mg/kg bw/day Carbosulfan in the diet for 24 months. Decreased body weights, increases in swollen or discoloured skin and biochemical changes indicative of reduced kidney function were noted at 27 mg/kg bw/day and above. Corneal opacities in the eyes were seen at the highest dose. Cholinesterase levels in plasma red blood cells and brain were reduced in rats given 27 mg/kg bw/day or more. The NOEL was 1 mg/kg bw/day.

Reproduction and developmental studies

In a three generation reproduction study, rats were given dietary Carbosulfan. Reduced body weights of adults and pups were noted at the highest dose, 25 mg/kg bw/day. Also at this dose reduced litter size, number born alive and ability to survive was noted.

When Carbosulfan was given to pregnant rats and rabbits throughout the period of foetal development, maternal toxicity was noted at doses of 20 and 10 mg/kg bw/day, respectively. The following effects were noted in rats: reduced body weights of dams (20 mg/kg bw), reduced foetal weights (10 and 20 mg/kg bw) and decreased bone formation of the sternebrae (20 mg/kg bw). In rabbits, three out of sixteen dams treated with 10 mg/kg bw died during the study and a slight reduction in body weights was also noted at this dose.

Genotoxicity

Carbosulfan did not show any evidence of genotoxic activity in assays for mutation in *Salmonella, Saccharomyces, Bacillus* and mouse lymphoma cells; and for chromosomal injury in mice or rats.

Human studies

Dermal doses of up to 16 mg/kg bw Carbosulfan for four hours in male volunteers resulted in a dose-related inhibition of red blood cell cholinesterase activity and signs of acute toxicity.

PUBLIC HEALTH EFFECTS

Poison Scheduling

The National Drugs and Poisons Scheduling Committee (NDPSC) considered the toxicity of Carbosulfan in 1989 and assessed the necessary controls to be implemented under States poisons regulations to prevent the occurrence of poisoning.

The NDPSC recommended that Carbosulfan be listed in Schedule 7 of the Standard for the Uniform Scheduling of Drugs and Poisons (SUSDP).

There are provisions for appropriate warning statements and first-aid instructions on the label of the product.

NOEL/ADI

The most sensitive species was the rat, with a NOEL of 1 mg/kg bw/day. 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 extrapolation of animal data to humans, variation within the human population; the quality of the experimental data; and the nature of potential hazards. Using a safety factor of 100, an ADI of 0.01 mg/kg bw/day was established for Carbosulfan.

Residues Assessment

Background

Carbosulfan is a broad spectrum carbamate insecticide registered in many overseas countries to control a number of soil and foliar pests in a range of crops including maize, cotton, rice, citrus, potatoes, and deciduous fruit Carbosulfan itself is non-mobile in plants in contrast to the mobile Carbofuran to which it readily converts and to which it is structurally related. Carbosulfan is substantially less toxic to mammals than Carbofuran.

The use being sought in Australia is for control of various pests in young and emerging cotton. Key aspects of the application are that Carbosulfan degrades to Carbofuran and that use of Carbofuran is already permitted in Australia.

An Australian maximum residue limit (MRL) for Carbofuran has been established for cotton seed at the limit of quantitation, 0.05 mg/kg. Animal and poultry commodity MRLs for Carbofuran are also at the same limit of quantitation, 0.05 mg/kg. There are currently, Carbofuran MRLs for bananas, maize, rice, sorghum, sugarcane, sunflower seed, sweet corn and wheat (between *0.05 and 0.2 mg/kg) as well as a primary (animal) feed commodity MRL of 2 mg/kg.

The applicant initially proposed a cotton seed MRL of 0.1 mg/kg as Carbosulfan but later amended this to a Carbofuran MRL of *0.05 mg/kg (equal to the current Carbofuran MRL for cottonseed) because of the conversion of the Carbosulfan to Carbofuran. A grazing restraint was also proposed.

Metabolism

Laboratory and farm animal and plant metabolism studies were presented.

Rats

In **rats** given a single oral dose of carbon 14 labelled Carbosulfan at 30 mg/kg body weight, whole body autoradiographs showed peak tissue concentration occurred at about 6 hours after dosing. After 24 hours, carbon 14 concentration in most tissues was described as minimal. After 48 hours, most of the dose had been eliminated in the urine or faeces with only liver and some glandular material having above background carbon 14 levels.

When rats were given a single oral dose of carbon 14 labelled Carbosulfan at 3 or 30 mg/kg body weight, 60-90% of the dose was excreted in the first 24 hours after dosing. Depending on the position of the radiocarbon in the Carbosulfan, the majority of the dose was eliminated from the urine or the urine and expired carbon dioxide. In the tissues, the liver was the site of highest residue levels.   Fat was not identified as a site of major residue deposition.

In rats given single or multiple doses of Carbosulfan at 4 mg/kg body weight or a single dose at 30 mg/kg body weight, the majority of the low dose residues were excreted within 48 hours and 72 hours for the high dose. Depending on the position of the carbon 14 in the

Carbosulfan, the majority of the dose was eliminated from the urine or from the urine and expired carbon dioxide.

Extensive metabolism of the Carbosulfan was indicated by the presence of a large number of metabolites in the urine and Carbosulfan and Carbofuran either being not detected or present in low levels. At 168 hours post-final dosing, mean radiocarbon levels in all tissues from treatment with Carbosulfan labelled in the dibutylamino group were ≤0.13 μg (parent equivalents)/g for the low dose tissues and ≤0.86 μg/g for the high dose tissues.

Residues in the tissues from phenyl ring carbon 14 labelled Carbosulfan were either not detected in high dose treated tissues or present at low levels only in kidneys and muscle of low dose treated animals. Because of the low amount of radiocarbon left in the carcasses and tissue/organs (<2% of the administered doses), tissues and organs were not analysed for metabolites.

The rat metabolism studies indicated rapid and extensive metabolism of Carbosulfan and (the resulting) Carbofuran occurred with no significant amounts of either compound being expected in tissues.

Lactating goats

Lactating goats were orally dosed with carbon 14 Carbosulfan for 7 consecutive days at 4.4 or 11.4 ppm in the feed. At slaughter, approximately 80% of the total administered radiocarbon was in the urine, 2-3% in the faeces, 0.6% in the milk, and 2-3% in the expired air for total recoveries of about 86% of the administered doses. In the milk, radioactivity reached a plateau by day 3. The average total radioactivity in whole milk plateau value was 0.016 ppm from the 4.4 ppm fed animal and 0.043 ppm in the milk from the 11.4 ppm fed animal.

Maximum residues were in the liver and kidney (0.031 and 0.05 (low dose) ppm and 0.11 and 0.12 ppm (higher dose) respectively). In the omental fat, total residues were approximately 0.006 ppm from both high and low dose animals. In the liver, kidney, and milk, concentrations of Carbosulfan, Carbofuran and their metabolite levels were low (<0.02 ppm).

In a second lactating goat study, two goats were fed at 10 ppm Carbosulfan in the feed for 10 days. At slaughter one of the goats had 79% of the administered dose in the urine, 2.7% in the faeces, 1.4% in the milk and 0.6% in the expired air for a total recovery of 84%. In the milk from both goats, total radioactivity reached a plateau after about 3 days (≈0.25-35 ppm total carbon 14 residues as Carbosulfan equivalents). The radiolabel cleared readily, after approximately 4 days of being on Carbosulfan free feed. The goat not killed at slaughter had a total radioactivity of 0.05 ppm in the milk.

In the tissues maximum residues were in the liver (total carbon 14 residues, 542 ppb, 0.1% of which was Carbosulfan and its metabolites) and kidney ((total carbon 14 residues, 611 ppb, of which 2.8% was Carbosulfan and its metabolites). Tissues residues showed evidence of depletion once exposure ceased. Levels of total carbon 14 in fat were much lower (7-12 ppm at time of slaughter, 19-28 ppm after approximately 4 days off treated feed). The low increase in fat residues was attributed to incorporation of the radiolabel into natural fatty acids. Carbosulfan and its metabolites were minor constituents of the radiolabelled material in tissues and milk with the largest Carbosulfan and Carbosulfan metabolite concentration being in the kidney (≈ 0.02 ppm).

The lactating goat studies show that Carbosulfan does not accumulate in milk or tissues, and is readily metabolised. Feeding at approximately 10 ppm in the feed for up to 10 days resulted in tissue and milk residue levels of 0.02 ppm or less of Carbosulfan or Carbofuran and their metabolites.

Plants

Carbosulfan residues in cotton and corn were shown to be readily metabolised, forming Carbofuran and 3-hydroxycarbofuran as principal metabolites following stem injection or painting onto leaves. In rice metabolism studies, soil applied Carbosulfan was readily degraded to Carbofuran which was taken up into the plants. Residues in mature rice grains from the soil application were low and essentially unextractable.

The plant metabolism studies show that residues of Carbosulfan readily undergo significant degradation when applied to the soil. The proposed treatment of the cotton seeds is by incorporation with the seeds into the soil at sowing and would not be expected to result in residues of Carbosulfan in harvested produce. Metabolism studies of the fate of radiolabelled residues in cotton seed planted with Carbofuran and grown to maturity were not presented. As the time between treatment and analysis increased, the percentage of unextractable residues increased and it would be expected that levels of Carbofuran and other metabolites would correspondingly decrease over time to inconsequential levels.

Analytical methods

Analytical methods are available for the determination of Carbosulfan, Carbofuran and 3-hydroxycarbofuran in cotton seed, cotton fodder, milk, and animal tissues.

Carbosulfan, Carbofuran, and 3-hydroxycarbofuran can be measured separately or as Carbofuran and 3-hydroxycarbofuran after hydrolytic conversion of Carbosulfan to Carbofuran. The determination of, and expression of Carbosulfan residues as Carbofuran and 3-hydroxycarbofuran is considered appropriate as no residues of the Carbosulfan itself are expected in the case of the soil applied use pattern.

The animal tissue analytical methodology presented determined Carbosulfan, Carbofuran, and the Carbofuran metabolites, 3-hydroxy and 3-keto Carbofuran. This was appropriate as cow feeding studies identified Carbosulfan and 3-hydroxy Carbofuran as the relevant residues in milk and tissues. In the case of treated cotton fodder being fed to cattle, no Carbosulfan would be expected to be present and measurement of Carbofuran and 3-hydroxycarbofuran alone should be appropriate under those circumstances.

The methods have acceptable specificity and sensitivity.

Storage stability

Studies specifically designed to show storage stability of residues in plants, animal tissues and milk were not presented. While this was considered of minor concern because the proposed use pattern is not expected to result in residues of significance, storage stability of residues has been identified as an issue needing further consideration by the FAO/WHO Joint Meeting on Pesticide Residues. Some indirect evidence was obtained showing that the principal metabolites, Carbofuran and 3-hydroxycarbofuran, are stable under storage conditions.

Residue definition

The plant metabolism studies, analytical methodology, and residue results support the residue definition for Carbosulfan being measured as 'Carbofuran' for this early season, soil application use pattern. This is considered appropriate for the proposed use pattern where Carbofuran and 3-hydroxycarbofuran are expected to be the only residues of consequence (the Carbofuran residue definition includes both Carbofuran and 3-hydroxycarbofuran residues). The Codex Alimentarius residue definition is the parent, Carbosulfan. Any extension of use of Carbosulfan to foliar applications or use patterns in which Carbosulfan could be expected to be present would require a review of the Australian residue definition.

Residue trials

Results from three Australian residue trials on cotton seed (including one which measured residues in cotton fodder and cotton trash) and one Brazilian cotton seed trial were presented. All the trials used the proposed use pattern or an equivalent. The residue levels in all the trials were between <0.02 and 0.05 mg/kg (as Carbosulfan) and allowed a conservative MRL of *0.05 mg/kg (as Carbofuran) for cotton seed to be recommended. This value is the same as that set for the current Australian Carbofuran cotton seed MRL. The residues in cotton trash and fodder were <0.05 mg/kg and required no change to the present primary feed commodities MRL of 2 mg/kg set for Carbofuran.

Withholding period and protection statement

No harvest withholding period statement is considered necessary because of the "at sowing" application. The protection statement, "DO NOT graze any treated area; or cut for stock food" is recommended to prevent inadvertent exposure of animals to residues.

Processing studies

The argument that Carbosulfan residues would not be of concern in processed products because of its conversion to Carbofuran residues was accepted. The argument that the physico-chemical properties of Carbofuran and 3-hydroxycarbofuran made oil accumulation unlikely was also accepted. Additionally the absence of significant residue levels in the cotton seed was taken as support for the contention that a processing study was not necessary.

Animal commodity MRLs

Results from an animal feeding study on lactating cattle fed at rates of 5 to 50 ppm Carbosulfan in the diet for 28 days indicated that at levels of up to 5 ppm in the feed, residues of Carbofuran and Carbosulfan in meat and milk are expected to be less than 0.05 mg/kg. Consequently no change to the current Carbofuran MRLs of *0.05 mg/kg for meat, mammalian and milks is required by the proposed use pattern.

Animal feed commodity MRL

Data presented on residue levels in cotton seed, cotton trash, and cotton fodder indicated that residues of Carbosulfan and Carbofuran are expected to be less than 0.05 mg/kg. Consequently no change to the current Carbofuran "primary feed commodities" MRL of 2 mg/kg was considered needed.

Estimated dietary intakes

The theoretical maximum daily intake (TMDI) calculated for Carbosulfan is <0.01% of the ADI of 0.01 mg/kg body weight/day.

Recommendations

Registration of the product

Registration of MARSHAL® 250 EC INSECTICIDE as a soil treatment applied at planting of cotton seed is supported on residue grounds.

Amendments to the *MRL Standard*

Table 1 of the MRL standard is amended by addition of reference to 'Carbosulfan' and to its being measured as 'Carbofuran'.

Carbofuran MRLs entries of *0.05 mg/kg for meat [mammalian], edible offal (mammalian), and milks are unchanged as is the Table 4 Carbofuran entry of the MRL of 2 mg/kg for "primary feed commodities".

Table 3 is amended by addition of the residue definition for Carbosulfan and amending the Carbofuran residue definition by adding a reference to Carbosulfan.

Recommended amendments to the *MRL Standard*

The following amendments to Tables 1, 3 and 4 of the *MRL Standard* are recommended:

Table 1

Compound	Food	MRL (mg/kg)
Add:		
Carbosulfan	see Carbofuran	Residues arising from the application of Carbosulfan to the soil at cotton seed planting are covered by the cotton seed MRL for Carbofuran.

Table 3

Compound	Residue
Add:	
Carbosulfan *see* Carbofuran	Residues arising from the application of Carbosulfan to the soil at cotton seed planting are covered by the cotton seed MRL for Carbofuran.
Delete:	
Carbofuran *see also* Furathiocarb	
Add:	
Carbofuran *see also* Carbosulfan and Furathiocarb	

Table 4

Compound	Animal Feed Commodity	MRL (mg/kg)
Add:		
Carbosulfan *see* Carbofuran	Residues arising from the application of Carbosulfan to the soil at cotton seed planting are covered by the primary feed MRL for Carbofuran.	

Withholding period and protection statement

No harvest withholding period statement is considered necessary because of the "at sowing" application. The following protection statement is recommended to avoid inadvertent exposure of animals to residues from grazing treated areas or being fed material from such areas:

PROTECTION STATEMENT: DO NOT graze any treated area; or cut for stock food.

Assessment of Overseas Trade Aspects of Residues in Food

Trade

Cotton, cotton seed, and cotton seed fodder are not expected to have measurable residues of carbosulfan or carbofuran as a result of the use of Marshal® 250 EC Insecticide. Absence of measurable residues indicates no trade concern is expected. The magnitude of the residues is consistent with the 0.02 and 0.1 mg/kg MRL values established for carbosulfan in cottonseed in Brazil and Spain and also means there is compliance with the present Australian carbofuran MRL for cottonseed of *0.05 mg/kg.

Because of the absence of measurable residues in cotton fodder and forage, animals fed treated cottonseed, meal, etc. are not expected to have measurable residues. This means there will be compliance with the Australian carbofuran animal commodities MRLs of *0.05 mg/kg.

This absence of measurable residues would also be expected to result in compliance with the USA's pending tolerances for carbosulfan and carbofuran tolerances in meat and meat by-products. While the USA's residue definitions for carbosulfan and carbofuran include metabolites not in the Australian residue definition, the Australian use pattern with its early season application could be expected to result in residues of such metabolites meeting the US levels. Analytical confirmation of this was not required in the Australian residue evaluation.

No carbosulfan MRLs have been established by the Codex Alimentarius Commission. The present Australian cottonseed MRL of *0.05 mg/kg established for carbofuran is consistent with the Codex oilseed MRL of *0.1 mg/kg. The Australian and Codex animal commodities MRLs of *0.05 mg/kg are comparable although different commodity classifications are used.

Occupational Health and Safety Assessment

Introduction

The active ingredient Carbosulfan is determined to be a hazardous substance by FMC International A.G. according to National Occupational Health and Safety Commission (NOHSC) Approved Criteria for Classifying Hazardous Substances. This classification is based on its acute oral and inhalation toxicity, and its potential for skin sensitisation. Substances containing Carbosulfan at 1% or above will be classified as hazardous.

Carbosulfan is an orange to brown clear viscous liquid with mild phenolic odour and low vapour pressure. It is Class a 6.1 dangerous good under the Australian Code for the Transport of Dangerous Goods by Road and Rail (ADG Code).

Marshal® 250 EC Insecticide (containing 250 g/L ai) has been classified as a hazardous substance by FMC International A.G. in accordance with NOHSC Approved Criteria based on its acute oral and inhalation toxicity, skin and eye irritancy and skin sensitisation. The product is an emulsifiable concentrate which will be formulated in Australia and available in 20 L steel drums with 50 mm steel bung or in 50 L returnable, refillable kegs with a closed valve system. The product is a Class 6.1 dangerous good under the Australian Code for the Transport of Dangerous Goods by Road and Rail (ADG Code).

Formulation, repackaging, transport, storage and retailing

Technical Carbosulfan will be imported into Australia and formulated into Marshal® 250 EC Insecticide. Transport drivers, warehouse personnel, plant operators, plant fillers and waste disposal operators will be involved in the formulation process. Closed systems will be used during mixing operations. Drum decanting and filling operations will be conducted under local ventilation. Waste disposal operators and workers involved in decanting and filling operations will be required to wear appropriate personal protective equipment. Transport and storage workers will only be exposed to the product if packaging is breached.

Advice on safe handling of Carbosulfan and Marshal® 250 EC Insecticide is provided on the respective labels and Material Safety Data Sheets (MSDS).

End use

Marshal® 250 EC Insecticide will be used to treat cotton seed at the time of planting only. It will be sprayed directly into the planting furrow over the cotton seed, using a 10 cm bandspray at a spray height of 15-20 cm, and covered immediately by soil. The application rate will be 20-40 ml/100 m row using 50-70 L water/ha. At this rate the most concentrated spray solution will contain 8% product (2% Carbosulfan).

Workers may be exposed to Carbosulfan when mixing/loading, applying spray and cleaning up spills and equipment.

The main route of exposure to Marshal® 250 EC Insecticide will be via skin contact. Inhalational exposure during spray application should not be significant given the application method and the low vapour pressure of the product.

The main occupational hazards associated with the product are skin and eye irritation, skin sensitisation and cholinesterase inhibition. Studies in male volunteers exposed dermally to Carbosulfan for 4 hours resulted in clinical signs of toxicity and a dose-related reduction in red blood cell cholinesterase activity. Carbosulfan may be absorbed through the skin.

Exposure studies submitted by the applicant were for use with hand held spray equipment in glass houses and were not relevant to the proposed use pattern in Australia. Exposure and risk when mixing and loading the product was estimated using the UK Predictive Operator Exposure Model (UK POEM).

The risk assessment indicated that workers mixing and loading from 20 L drums will be exposed to unacceptable levels of product. However, these workers are expected to be adequately protected if they use the 50 L refillable kegs proposed by the applicant, and suitable protective clothing (overalls, hat, PVC gloves and face shield or goggles). A qualitative risk assessment showed that the product can be applied safely provided appropriate protective equipment (overalls, hat and PVC gloves) is worn.

Entry into treated areas or handling treated crops

The product will be applied to soil only. On soil, Carbosulfan will rapidly degrade to its more toxic metabolite, Carbofuran, as well as other related chemicals. However once taken up by the plant they will be metabolised to larger forms (conjugated with plant sugars) which will not be absorbed by the body.

Workers such as cotton chippers, crop checkers, growers and advisers may enter or handle treated crops. The main source of exposure will come from contact with treated soil. The health risk to crop checkers and other re-entry workers who handle foliage only is expected to be low. Dermal contact with soil may result during cotton chipping, however, this activity will be conducted approximately 8 weeks after planting, by which time soil residue levels will be minimal. Harvesting and handling of harvested cotton will be conducted mechanically and should not result in worker exposure.

Recommendations for safe use—all workers

Formulation and packaging

The applicant has indicated that a number of control measures are currently in use in the formulation plant. Workers at the formulation plant should continue to be protected by adequate ventilation, closed systems and the use of suitable personal protective equipment. Workers involved in drum decanting and rinsing should continue to wear chemically impervious suits, air hood, PVC boots and nitrile gloves. Workers at the plant filler should continue to wear a PVC apron, face shield, PVC boots and nitrile gloves. In addition to these controls special training should be made available to all workers involved in product formulation.

End users

End users should follow the instructions and Safety Directions on the Product label. Workers mixing and loading Marshal® 250 EC Insecticide should wear cotton overalls buttoned to the neck and wrist and a washable hat, elbow-length PVC gloves and face shield or goggles. Applicators should wear cotton overalls buttoned to the neck and wrist and a washable hat and elbow-length PVC gloves.

Personal protective equipment

The personal protective equipment worn by all workers should meet the relevant Standards Australia standard specified below:

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

Goggles - AS 1337-1992, Eye Protection for Industrial Applications

Overalls and aprons - AS 3765-1990, Clothing for protection against hazardous chemicals

Footwear - 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

Active constituent label

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

MSDS

Manufacturers and importers have produced MSDS for Carbosulfan and Marshal® 250 EC Insecticide. 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 them.

Packaging restrictions

Based on the risk assessment, the use of 20 L product containers will not provide adequate protection from exposure during mixing and loading operations. The product should only be available in closed systems, therefore, use of the following container only is supported:

50 L refillable keg equipped with closed valve system

Conclusions

Worksafe Australia supports registration of Carbosulfan in Marshal® 250 EC Insecticide at 250 g/L as an emulsifiable concentrate for use as a pre-emergence insecticide in cotton, on the condition that:

- the product is packaged in 50 L refillable kegs equipped with closed valve system, and
- the application is by in-furrow method only (product sprayed directly into planting furrow from a nozzle mounted low on the planting equipment and covered immediately by soil).

Environmental Assessment

Environmental fate

Marshal® 250 EC Insecticide is an emulsifiable concentrate containing Carbosulfan as its TGAC. Carbosulfan is a systemic broad spectrum carbamate insecticide which is used to control a number of soil and foliar pests. Marshal® 250 EC Insecticide is recommended for use in cotton at planting to control early season insect pests such as thrips, jassids, wireworms, leafhoppers and green mirids.

Degradation

Hydrolysis

Four studies on the aqueous hydrolysis of Carbosulfan were presented by the applicant, two of which were scientific papers. Results of all studies indicate that Carbosulfan is rapidly hydrolysed to Carbofuran in water under acidic and neutral conditions, but more slowly in basic conditions.

Half lives determined in one study for Carbosulfan were 0.2, 11.4 and 173.3 h for pH of 5.0, 7.0 and 9.0 respectively. This compares with half lives at pH of 3, 5, 7 and 9 of 0.15, 2.9, 256 and 797 hours from one of the literature studies

A second report, while showing the same stability for Carbosulfan as above, indicated a significant effect on the rate of hydrolysis depending on the initial concentration of Carbosulfan, with the rate decreasing at higher concentrations (0.5-5 mg/L).

Photolysis

The photolysis of Carbosulfan was studied on dry soil, moist soil and in buffered water with radiolabelled material incorporated into either the aromatic ring or the dibutylamine side chain. This study was not performed to current standards and did not follow recognised national or international guidelines.

The results in the dry and moist soils using ring labelled Carbosulfan showed that the rate of loss of Carbosulfan and the formation of Carbofuran in the irradiated and control samples were very similar and there was no significant difference in the degradate. It was concluded that irradiation had very little effect on the breakdown of Carbosulfan in the soil used with hydrolysis being responsible.

As there was no evidence given that the soil was sterilised before it was used and the soil had a low pH, in which the hydrolysis of Carbosulfan is fast, the experiments are not considered to be valid for determining the extent of photolysis of Carbosulfan on soil.

The aqueous photolysis of Carbosulfan was performed in buffer at pH 7.0 or in distilled water, with the samples exposed to the UV light for 8 days.

The results in the buffered water gave half lives of 1.33 days and 1.44 days with half lives in the control samples of 7.5 days and 10.5 days for the ^{14}C-ring and ^{14}C-DBA respectively.

The results from the distilled water samples were almost identical to the buffered water situation but the half lives were considerably longer, 3.89 and 8.25 days with controls 21.7 and 34.7 days for ring labelled and DBA labelled materials respectively. The metabolites and their concentrations was also very similar to that in the buffer experiment when allowance is made for the slower rate of degradation.

Metabolism

Aerobic soil metabolism

The metabolism of Carbosulfan under aerobic conditions was studied in sandy clay loam and silt loam soils where the degradation was fast with half lives of <1 day and 5 days respectively. The only metabolite was Carbofuran which was then slowly metabolised to other products. This is an old report and was not performed or reported according to modern protocols. However, the results are considered reasonable.

Anaerobic soil metabolism

The anaerobic study was performed using the same soils as above and again not to modern standards. The study started with aerobic conditions for approximately the first half life (one day for the silt loam and 3 days for the other soil), then the soils were flooded with degassed water to initiate the anaerobic conditions. Under these conditions a half life for the metabolism of Carbosulfan to Carbofuran could not be determined. However, it was clear that degradation of Carbosulfan was occurring to give Carbofuran. The Carbofuran produced was very slowly degraded further.

In a study reported in the literature the aerobic and anaerobic metabolism of Carbofuran in a sandy loam soil was reported. The aerobic degradation of Carbosulfan showed that the half life was 3 days and that the dibutylamine produced was quickly incorporated in the organic fraction of the soil or mineralised to CO_2. The anaerobic study was performed by storing the soil under anaerobic conditions before adding the test compound and deoxygenated water. The half life of Carbosulfan was determined to be about 2 days. Again, there was little significant further degradation of Carbofuran which was stable.

Aerobic aquatic metabolism

No aquatic metabolism studies were presented by the applicant. Given the rapid hydrolysis and the observation that in the soil metabolism studies that the rate of degradation of Carbosulfan to Carbofuran was a non-biological process, it is expected that in natural waters Carbosulfan will degrade to Carbofuran by hydrolysis and that the rate of degradation will not be significantly changed in biologically active water. Also, little is expected to reach water from the proposed application method. The lack of an aquatic metabolism study is therefore acceptable in this case.

Mobility

The adsorption of Carbosulfan, Carbofuran and dibutylamine was determined in four soils using conventional methods, although testing was not performed to current guidelines. Three concentrations per compound were used and the Freundlich constants determined.

The results indicate that Carbosulfan can be considered to have low to slight mobility, dibutylamine can be considered to have high to medium mobility, while Carbofuran can be considered very highly mobile in soil. Carbosulfan has an adsorption range of K_{oc} 1667-2691, and a desorption range of K'_{oc} 2095-4758, indicating that once sorbed, the compound does desorb slowly.

The column leaching study was also not performed to current guidelines, but the method used is very similar to the US EPA Guidelines for aged soil column leaching. Carbofuran, the major metabolite, was in the leachates from the sandy loam and fine sand soils. However, it not did not leach to the same extent from the silt loam soil column but was found throughout the column. This is likely to be a result of a significantly higher clay and silt content than found in the other tested soils.

The results from the column study do suggest that the compound degrades quickly, and the metabolite Carbofuran is conducive to leaching.

However, a two year lysimeter study finalised in 1992 suggests otherwise. The field lysimeter study was performed in duplicate using two undisturbed soil cores.

At the end of the study there was 0.76% and 0.78% of the applied radioactivity recovered in the leachates for lysimeter 1 and 2 respectively with the remaining quantities of radioactivity found at day 740 of the study in the soil cores being 30.3% and 29.6% in lysimeters 1 and 2 respectively. No radioactivity was detected below 40 cm. This suggests in both cases during the 2 year period of the study, approximately 70% of the applied radioactivity passed into the atmosphere indicating that mineralisation of the main metabolite Carbofuran to CO_2 played a dominant role.

The GUS monograph scores were 0-0.54 for Carbosulfan (half life of <1-5 days in soil, Koc of 1667-2619) and 3.6-5.3 for Carbofuran (half life of 30-60 days in soil, Koc of 10.5-37). These scores indicate that Carbosulfan is a probable non-leacher, while Carbofuran is a probable leacher.

However, the lysimeter results would show that Carbofuran is unlikely to leach from most Australian soils with the two year lysimeter study showing that Carbosulfan and Carbofuran are unlikely to leach below 40 cm and that significant degradation occurs.

Field dissipation, accumulation

Results from a model rice paddy ecosystem, prepared in an aquarium were presented. There was no analysis for individual metabolites or parent compound. The relevant conclusion from this study is that most of the applied radioactivity on the plants moved quickly into the soil and water compartments.

<u>Accumulation</u>

Three monthly applications of ring labelled Carbosulfan was applied to a silt loam soil at rates lower than those proposed in Australia. In the samples taken during application, only the total radioactivity in the soil cores was determined, and as such is of limited use. The other soil cores (tested at intervals after final application) were analysed for non-polar, polar and bound radioactivity, with most recovery found in the bound fraction.

Bioaccumulation

A fish accumulation study under flow-through conditions was performed using radiolabelled Carbosulfan. The bioaccumulation factors were determined as 730, 1100 and 990 for fillet, viscera and whole fish, respectively. At the end of the 30 days depuration phase, 60%, 72% and 72% of the accumulated residues were eliminated from the fillet, viscera and whole fish respectively, indicating incomplete depuration after this relatively long time scale. There was no analysis of what the ^{14}C residues in the fish tissues. As the label was in the dibutylamine group, these residues are not expected to be Carbofuran. However, results in a thesis study show that Carbofuran is the major metabolite formed in fish.

Radiolabelled Carbosulfan was also added to soil, then the soil aged aerobically before being flooded with aerated water. The system was allowed to equilibrate (7 days) before fish were added. At the end of the soil ageing concentration of Carbosulfan was 0.42 μg/g soil and Carbofuran 0.31 μg/g soil.

There was limited bioaccumulation of radioactive residues in the fish tissues, with bioaccumulation factors of 8, 11 and 14 for fillet , whole fish and viscera, respectively. The BCFs are based on total radioactivity. There was no chemical analysis of the residues in the fish and soil but analysis of the water phase showed that concentration of Carbosulfan was <0.10 μg/L (limit of detection) and Carbofuran was 7.9 μg/L.

The above studies are of limited value and raise some concerns. However, a more definitive test will not be requested due to low aquatic exposure expected.

Environmental effects

Results using the TGAC for the following are available: birds, fish, aquatic invertebrates and bees. Some data can be gained for effects on mammals and non-target terrestrial plants from toxicological and plant accumulation studies. The following gives summaries of the studies in this area.

Avian toxicity

Carbosulfan is highly acutely toxic to ducks (LD50=8.1 mg/kg) and likely to be to most bird species. The dietary LC50s show that ducks are more sensitive than quail or pheasants (the LC50s are between 1,000-2,150 ppm (nominal) for quail and pheasants and 100-215 ppm for mallards). While these studies are old and not performed to current standards, they are considered to be reasonably well performed and reliable.

A field study, performed in the UK, was reported in which the number of birds before and after seeding of sugar-beet using Carbosulfan (Marshal 10G) at 3 g ai per 100 m row (approximately 30% of the proposed Australian rate) were determined. There was no significant difference in the bird population that could be attributed to Carbosulfan before and after seeding. The number of species in the morning did not change pre seeding to post seeding but the number of individual birds seen decreased slightly, and was considered to be due to changes in the season and other variables.

Aquatic toxicity

Results from aquatic testing showed Carbosulfan to be very highly toxic to fish and *Daphnia*. LC50s were determined as 14.9 and 15 ppb for bluegill sunfish, 42.4 and 129 (flow through testing on formulation) for rainbow trout and 2.4 and 1.5 ppb for *Daphnia magna*. Hydrolysis of Carbosulfan to Carbofuran is expected, and results could reflect the metabolite. However, at the pH of solutions used in testing (6.6-7.5), the half-life of Carbosulfan is expected to be 11 to 256 hours. With most mortalities in the fish studies occurring within 24 to 48 hours, it is likely the toxic effects are a result of the parent compound. Similarly with *Daphnia*, most immobilisation at the EC50 concentration occurred between 24 and 48 hours. Nonetheless, all results, including those of the flow-through test, are in nominal concentrations, and should be treated with some caution.

As all of these results are in nominal concentrations, indicating they have to be treated with some caution.

No sublethal effects were observed (or recorded) during testing on *Daphnia*. Carbosulfan can be classed as very highly toxic to fish and *Daphnia*.

Non-target invertebrates

Contact toxicity testing on bees indicates Carbosulfan is toxic to bees, with an LD50 of 0.685 μg per bee. However, further field tests showed that toxicity is only likely to occur if bees are caught in the spray path. Bees placed in sprayed foliage 2 hours after application had no mortality, indicating there was no fumigant effect.

Carbosulfan was found to not adversely affect the level of nitrate present in treated soils, even with treatment levels at 10 times those proposed for use in Australia. Also at these high rates, Carbosulfan was shown to not adversely effect the rates of degradation of cellulose, starch and protein.

Phytotoxicity

Carbosulfan is considered to be non-phytotoxic to plants when applied as a foliar application to a wide range of plants.

PREDICTION OF ENVIRONMENTAL HAZARD

Hazard arising from use

Marshal® 250 EC Insecticide will be used as an in furrow spray, applied at the time of planting. The spray nozzle used will deliver a coarse spray in a 10 cm band over the cotton seed before soil is brought in behind covering tynes in front of the press wheel. This process will result in minimal exposure to the environment.

Terrestrial organisms

Birds

There will only be 1 application per year where 10 g ai per 100 m row is applied at the time of planting, equating to 1000 g ai/ha, while the effective rate in the treated areas is 10 kg ai/ha. Exposure to birds will be expected to be very low, as covering with soil immediately after application will mean no chemical is available for consumption, except for birds eating cotton seedlings or foraging in the sprayed band. Calculations show birds would need to eat a large amount of seed spread over a wide area to consume a toxic dose.

However, the main metabolite, Carbofuran, has been known to cause bird deaths when used in granular formulations. While it is claimed that soil dwelling insects killed by Marshal® 250 EC would generally remain in the soil and would be unlikely to be found and consumed by birds, although this claim is not substantiated. Environment Australia is seeking monitoring data from the company on this issue, and on bird species (eg galahs and corellas) and their habits frequenting cotton crops.

Bees

Whilst Carbosulfan can be considered highly toxic to bees, the timing of application is at seeding of cotton, so no flowering activity will be present. Additionally, the method of application is such that spray drift should be an absolute minimum, and no dermal contact with bees could reasonably be expected. The hazard to bees can be described as low.

Soil dwelling invertebrates

Carbosulfan has such a short half life in aerobic soils (1-5 days) that there is not expected to be any accumulation of this chemical. Additionally, only around 10% of the cropped area will be exposed to the chemical at application. This leaves 90% of the area available untreated, and should provide an adequate reserve for soil invertebrates, thereby lowering the hazard, in spite of the toxic Carbofuran being formed. Additionally, populations of natural invertebrates in freshly cultivated cotton fields are likely to be low.

Aquatic organisms

Aquatic organisms are unlikely to come in contact with Carbosulfan as a result of direct overspray. All spray is directed into the furrow contacting bottom, sides and all soil drawn into the furrow at closure. Therefore, spray drift can also be expected to be negligible. Even exposure through soil runoff is expected to be low because of this application method.

Assuming 1% runoff with soil from a heavy rain event (60 cm) a Q value can be determined as 0.35 to fish (based on most sensitive result) and 3.47 to *Daphnia*. This indicates an unacceptable risk using the above scenario to *Daphnia magna*, and a potential hazard to fish, although this may be reduced by mitigating factors.

The main metabolite, Carbofuran, is also known to be toxic to aquatic organisms, and is highly mobile. If all applied Carbosulfan were to metabolise to Carbofuran, then in 1 to 3 weeks, 1000 g/ha would be present. 10% of this reaching a 15 cm, 1 ha standing body of water would result in a concentration of 7 µg/L, which gives Q values of 0.95 to fish (an unacceptable risk), and 0.46 to *Daphnia* (potentially hazardous to this species). This risk is likely to be mitigated as discussed below.

There is between 10 to 15 cm of soil either side of the treated area of soil which will erode before the treated soil is exposed to water. Additionally, a further 2-5 cm of soil is on top of the treated band which must erode before exposure of treated soil. Even in the event of a heavy rainfall event, it is unlikely this much soil will be eroded straight away, but no figures are available to support this.

Furthermore, the lysimeter study provided with this submission (p 14) provides sound supporting evidence that Carbosulfan and Carbofuran remain in the soil column for extended periods of time, with neither found in significant quantities below 40 cm after a two year trial. With the mounds used for planting being around 30 cm high, this suggests little leaching of either chemical to the level of the irrigation ditches. Finally, the soils used in the study had a much higher sand content than NSW and Queensland cotton growing soils, indicating an even lower expected level of mobility in these areas.

Nonetheless, the above calculations do indicate a potential hazard to the aquatic environment which can not be ignored without quantitative data and monitoring data has been requested from the company.

Desirable vegetation

Carbosulfan is applied in a manner where it is unlikely to reach non-target vegetation. It is considered to be non-phytotoxic to plants when applied as a foliar application to a wide range of plants (Tomlin, 1994), and is not expected to pose a hazard in this regard.

PROPOSED USE

The hazard assessment has identified a potential environmental concern to birds, fish and *Daphnia*. The calculations were based on worst case assumptions, but in the absence of more accurate information, this is considered necessary. Information that would clarify hazard was sought at the time of assessing Carbosulfan for a permit application, but this request was not forwarded to the company. Because of this, and in light of the hazard assessment, the company has now agreed to:

1. Monitor the crop in the first year of application and report incidences of exposure and wildlife (particularly avian) poisoning arising as a result of the use of this product. Observations will include an indication of bird species frequenting the cotton crops and their habits, and whether dead or dying insects rise to the surface where they may be ingested.
2. Monitor representative tail waters resulting from irrigation or run-off after rainfall events in the first year of application and analyse for Carbosulfan and Carbofuran. Reports will indicate when events such as irrigation or storms occurred and also outline the analytical sensitivities used.

Efficacy and Safety Assessment

Early insect control in cotton is very important in order to maintain cotton vigour and stand and not prolong the time to maturity. This promotion of "earliness" has assumed a measure of importance to reduce growing costs and reduce the risk of weather damage at the end of the season. Insecticides such as aldicarb and phorate have been promoted and widely used by cotton growers to achieve these results.

Marshal® 250 EC is a product which contains carbosulfan, a systemic carbamate insecticide which is widely used in a range crops overseas for early control of soil and sucking insects. A number of formulations are in use.

Since 1989, 15 trials have been conducted in various cotton growing districts of New South Wales and Queensland to evaluate the eff'cacy and crop safety of Marshal® 250EC in irrigated cotton. This work has shown that the product has good potential for use in cotton. It has lower toxicity than the standard currently used products.

The claims for use for Marshal® 250 EC are for control of a range of early season soil and sucking insect pests of cotton when applied as an in-furrow spray treatment at planting.

Adequacy of efficacy data

Trial design in relation to provision of controls, treatment group size and number of replicates were of an acceptable scientific standard.

The experimental conditions in relation to pest pressure were quite adequate for the experimental work conducted. Weather conditions and soil type were consistent with what can be expected in the major cotton growing areas. The information was well researched, analysed and presented. The trial data is applicable to the use of the product under commercial conditions.

Claims

Thrips

A sound case has been presented for the use of Marshal® 250EC as an in-furrow treatment for the control of thrips in cotton. The data for thrips control clearly demonstrate the efficacy of carbosulfan for this purpose. Results were mostly equivalent to or better than the standard treatment.

Other sucking pests

Supporting data for jassids, leafhoppers and green mirids were each obtained from only one trial. The results confirm the expectations of the product given its systemic activity, and any further trials would almost certainly reinforce these data. Sampling difficulties were indicated in the case of highly mobile pests such as leafhoppers. Mirids were also highly mobile but the trial data show clear evidence of low numbers on the treated plots compared to the untreated. It should be noted that activity against these pests for greater than 28 days after sowing was not evaluated and probably should not be expected. This period of control is adequate for thrips, jassids and leafhoppers, but in the case of green mirids additional control would be required during the early squaring phase when the effects of in-furrow application have lapsed.

False wireworm

Four trials investigated the use of Marshal® 250 EC as an in-furrow spray for false wireworm control. Data from two of these trials provided evidence of efficacy against false wireworm larvae from results expressed as larval counts, plant damage and plant stand counts. In two of the trials there were relatively minor and non-significant differences in assessment criteria between top rate Marshal® 250 EC treatment and the untreated.

Sugarcane wireworm

There were data from only one trial to support the inclusion of sugarcane wireworm control. However, these data provided good evidence of efficacy against this pest. This trial had both false wireworm and sugarcane wireworm infestation. In view of the difficulty of gathering sound data on efficacy against soil insect pests, this data provided adquate evidence to support this claim.

Crop safety

Measurements and observations on crop safety of Marshal® 250 EC were carried out in all trials conducted. Marshal® 250 EC was included at 2.0 kg a.i./ha which is twice the intended commercial rate, in 7 of the 15 triais that were conducted. Assessments for plant stand, plant dry weight and visual crop damage were conducted in all trials. In three trials seed cotton yields were measured.

There was no evidence of any crop damage measured or observed from Marshal® 250 EC in any of the trials conducted. Negative effects on crop emergence and subsequent plant growth were not seen in any of the trials.

Marshal® 250 EC was shown to be safe to cotton when applied as an in-furrow spray at planting at rates of application up to 2.0 kg a.i.tha, which is twice the rate of the highest intended commercial rate of application.

Justifications for use and recommendations

This product allows for use of a less toxic chemical than the presently registered products. If applied as directed, Marshal® 250EC will perform as well as standard treatments for the uses specified in this application for registration.

Proposed Draft Label

Main Panel

DANGEROUS POISON

KEEP OUT OF REACH OF CHILDREN

READ SAFETY DIRECTIONS BEFORE OPENING OR USING

MARSHAL® 250 EC

Insecticide

Active constituent: 250 g/L CARBOSULFAN
(AN ANTI-CHOLINESTERASE COMPOUND)
Solvent: 605 g/L LIQUID HYDROCARBON

For the control of thrips, jassids, wireworms, leafhoppers and green mirids in cotton.

50 Litres

F M C *

FMC International AG
Suite 7, 36 Bryants Road
LOGANHOLME Q 4129

*FMC and Marshal are Registered Trademarks of FMC Corporation, Philadelphia, USA

PROPOSED DRAFT LABEL - MARSHAL 250 EC INSECTICIDE

ANCILLARY PANEL 2

GENERAL INSTRUCTIONS:

Marshal 250 EC is a soil applied systemic insecticide. It should be used as a soil treatment applied at planting to protect emerging cotton shoots from thrips, jassids and wireworms.

APPLICATION

Marshal 250 EC Insecticide is applied as a band spray to the open furrow at planting. Spray the entire furrow width (approximately 10 cm wide) using an even fan nozzle located directly behind the seed tube but infront of the covering tyne and press wheel. Ensure all the spray is directed into the furrow contacting bottom, sides and all soil drawn into the furrow at closure. Use 50 to 70 L of water/ha. Thorough coverage is essential.

MIXING

Add the required quantity of Marshal 250 EC to water in the spray tank and mix thoroughly. Maintain agitation during mixing and application.

PROTECTION OF WILDLIFE, FISH, CRUSTACEA AND THE ENVIRONMENT

Dangerous to fish and aquatic organisms. Do not contaminate dams, rivers, streams, waterways or drains with product or the used container. Tail drains which flow from treated areas should be prevented from entering river systems.

STORAGE, SPILLAGE AND DISPOSAL AND CONTAINER RE-USE

Store in original containers, in a cool well ventilated area away from children, animals, food and feedstuffs. Do not store for prolonged periods in direct sunlight.

In case of spillage, confine and absorb spilled product with absorbent material such as sand, clay or cat litter and dispose of waste as indicated below or according to the Australian Standard 2507 - Storage and Handling of Pesticides.

Empty containers fully into application equipment. Close all valves and return to point of supply for refill or storage.

SAFETY DIRECTIONS

Poisonous if absorbed by skin contact, inhaled or swallowed. Will irritate the eyes and skin. Repeated exposure may cause allergic disorders. Sensitive workers should use protective clothing. Avoid contact with eyes and skin. Do not inhale vapour or spray mist. When preparing spray wear cotton overalls buttoned to the neck and wrist and a washable hat, elbow-length PVC gloves and face shield or goggles. When using the prepared spray wear cotton overalls buttoned to the neck and wrist and a washable hat and elbow-length PVC gloves. If product or spray on skin, immediately wash area with soap and water. If product in eyes, wash it out immediately with water. After use and before eating, drinking or smoking, wash arms, face and hands thoroughly with soap and water. Obtain an emergency supply of atropine tablets 0.6 mg.

FIRST AID

If poisoning occurs, contact a doctor or Poisons Information Centre. If swallowed, give one atropine tablet every 5 minutes until dryness if the mouth occurs - if poisoned by skin absorption or through lungs, remove any contaminated clothing, wash skin thoroughly and give atropine tablets as above. Get to a doctor or hospital quickly.

WARRANTY

FMC makes no warranty express or implied, concerning the use of this product other than that indicated on the label. Except as so warranted the product is sold as is. Buyer and user assume all risk of use and/or handling and/or storage of this material when such use and/or handling and/or storage is contrary to label instructions.

BATCH NO. **DATE OF MANUFACTURE**

MSDS NO. FMC/MAR/1.

PROPOSED LABEL CLAIMS - ANCILLARY PANEL 3

MARSHAL 250EC INSECTICIDE

Directions For Use

Restraint : DO NOT apply under rough or dry soil conditions.

CROP	PEST	STATE	RATE[1]	CRITICAL COMMENTS
Cotton	Thrips (*Thrips* spp)	Qld, NSW and WA	2-4 L/ha OR 20-40 mL/100 m row	Apply as a spray into the furrow at planting. Use the higher rate for longer residual control. Use a spray nozzle which will deliver a coarse spray in a total volume of 5-7 mL/metre of row in a 10 cm band over the seed before soil is brought in behind covering tynes in front of the press wheel. Plant into moist warm soil conditions to allow rapid plant germination and uptake of Marshal 250EC for thrip control. If planting into marginal soil moisture irrigate as soon as possible after application.
	False wireworm, (*Pterohelaeus darlingensis*) Sugarcane wireworm (*Agrypnus variabilis*)		3 L/ha OR 30 mL/ 100 m row	Apply as above
	Jassids, (*Austroasca* spp) Cotton leafhopper, (*Amrasca terraereginae*) Green mirid (*Creontiades dilutus*)		4 L/ha OR 40 mL/ 100 m row	Apply as above

1. The per hectare rates are based on a 1 metre row spacing. Adjust the rate to 20, 30 or 40 mL/100m of row, as stated, for other row spacings.

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

Withholding Period: DO NOT ALLOW STOCK TO GRAZE TREATED COTTON.

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 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.