Public Release Summary

on

DIMETHOMORPH

in the product

ACROBAT MZ 690 FUNGICIDE

National Registration Authority
for Agricultural and Veterinary Chemicals

1997

(Published on the APVMA website on 14 October 2011 with a compete table of contents added)

Canberra
Australia

ISBN 0 642 26475 9

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

Mr Max Darvill
National Registration Authority for Agricultural and Veterinary Chemicals
PO Box E 240
KINGSTON ACT 2604

Ph: (06) 271 6549

Fax: (06) 272 3218

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. The publication of public release summaries for all products containing new active ingredients is part of that process.

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 occupational health and safety aspects, environmental impact, and residues in food are available from the NRA on request.

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

SUMMARY

The National Registration Authority for Agricultural and Veterinary Chemicals (NRA) has considered an application to register the new chemical dimethomorph which is to be combined with mancozeb for the control of various fungal diseases of cucurbits, lettuce, onions and potatoes in all States and Territories as specified in the directions-for-use table on the product's label.

This publication outlines the regulatory considerations and summarises the data reviewed by the NRA for the proposed registration of dimethomorph. Before deciding whether to approve this product for use in Australia, the NRA invites public comment. Comments should be submitted by 8 April 1997 to the NRA at the address indicated on page 1.

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

Agricultural aspects

ACROBAT MZ 690 FUNGICIDE is a wettable powder combination product containing 90 g/kg of the new morpholine fungicide, dimethomorph, and 600 g/kg of the commonly used protective fungicide, mancozeb. The new product has been developed in an attempt to delay the onset of fungicide resistance to dimethomorph, which is potentially a risk when systemic products are used alone.

The product is for use by ground sprayer and has been shown, when applied at 2.0 kg of product per hectare, to give good control of:

- downy mildew, anthracnose, gummy stern blight, altenaria leaf spot and septoria spot of cucurbits;
- downy mildew, anthracnose and septoria leaf spot of lettuce;
- downy mildew, leaf blight and purple blotch of onions; and
- late blight and early blight of potatoes.

Environmental aspects

The environmental hazard of dimethomorph will be highest to organisms living in the vicinity where the chemical will be applied in conjunction with mancozeb as part of a regular protectant spray program against various fungal diseases in cucurbits, lettuce, onions and potatoes in various States. Residues would be expected on plant surfaces, including the crop canopy, crop itself and inter-row plant cover, and on soil invertebrates exposed to spray. Surface water, uncultivated land and nearby non-target plants (e.g. trees and grasses) may be exposed through overspray, spray drift and/or run-off.

Dimethomorph does not hydrolyse and only slowly photodegrades in water and on soil surfaces. It has a moderately persistent half-life in aerobic soil biodegradation studies, while anaerobic studies showed a rapid initial degradation followed by a significant slowing down.

Biodegradation was rapid in two aerobic sediment-water systems, with half-lives for parent compound of 2.09 and 2.94 days in the whole system and disappearance of parent from water after 7 days after treatment (DAT) with no detections in sediment at ≤29 DAT. Field dissipation studies confirmed the moderate persistence as well as shifts in the E:Z isomer ratio from approximately equal to 1:3 in favour of the fungicidally active Z isomer. Mobility in soils was generally low to medium, and soil column studies showed that parent compound was not leached through a 30 cm soil column and remained mostly within the top 10-15 cm of soil.

The moderate persistence of dimethomorph may result in a 2.6% annual carryover and predicted residues of 28.1 g a.i./ha (equivalent to 0.014 mg a.i./kg soil in the top 15 cm) in the soil after one year given a maximum of six applications in a season on grapes. Plants can take up and translocate dimethomorph, although this is reduced as the compound is aged in soil. Bioconcentration is not expected due to the relatively low log K_{ow} of 2.63 and 2.73 for the E and Z isomers, respectively.

Dimethomorph was practically nontoxic to bobwhite quail and mallard duck in single oral dose and 5 day dietary toxicity studies. When tested alone, it was moderately toxic to rainbow trout and bluegill sunfish and only slightly toxic to carp. However, in conjunction with mancozeb as ACROBAT MZ 690 FUNGICIDE, it was very highly toxic to trout. No acceptable study was submitted on the toxicity of dimethomorph alone to daphnids, but as ACROBAT MZ 690 FUNGICIDE it was highly toxic. Dimethomorph alone was only slightly toxic to a freshwater green algae.

Dimethomorph is also relatively nontoxic to adult worker honey bees (orally and topically), earthworms, predatory mites and other beneficial arthropods. Soil nitrification, ammonification and respiration were not significantly affected at up to 10X the maximum rate (2.4 and 16 mg per kg soil of dimethomorph and mancozeb, respectively).

The proposed use of ACROBAT MZ 690 FUNGICIDE is not expected to pose an unacceptable hazard to birds, earthworms, bees, plants or soil microorganisms. While dimethomorph alone is only moderately toxic to fish, ACROBAT MZ 690 FUNGICIDE is highly toxic to both fish and daphnids in acute and chronic exposures. However, an assessment of the Q values indicates that an unacceptable acute hazard may exist only to fish from both a single direct overspray or 10% spray drift. Aquatic biodegradation studies show low persistence for both active constituents indicating no chronic hazard to aquatic animals is expected from repeated spraying.

The hazard from spray drift from the proposed use pattern of ACROBAT MZ 690 FUNGICIDE on cucurbits, lettuce and onions is expected to be acceptable if tractor-mounted boom sprayers producing large droplet sizes are used. The aerial application to potatoes presents a potentially unacceptable hazard to fish from both spray drift and direct overspray and should not be allowed unless further data are presented to demonstrate a reduction in hazard. In the

interim, only ground-based spraying using equipment and practices which minimise drift should be allowed.

Toxicology

The product ACROBAT MZ 690 FUNGICIDE is a wettable powder formulation containing the two active ingredients, dimethomorph at 90 g/kg and mancozeb at 600 g/kg, intended for use as an agricultural fungicide to combat the emergence of mancozeb resistance.

Dimethomorph is a new active constituent to the Australian market and has low acute oral, dermal and inhalational toxicity, is a slight eye irritant, but is not irritating to the skin. The formulation ACROBAT MZ 690 FUNGICIDE also exhibited low oral, dermal and inhalational toxicity consistent with the known low toxicity for mancozeb, the predominant active ingredient by weight, and the demonstrated low toxicity of dimethomorph. The formulation is not a skin irritant and is a slight eye irritant. Australia has no evidence of skin sensitisation by mancozeb; however, ACROBAT MZ 690 FUNGICIDE is assumed, on the basis of an evaluation by a foreign agency and until specific studies are provided, to be a skin sensitiser.

In short-and long-term studies, the primary manifestations of dimethomorph toxicity were nonspecific clinical signs and reduced weight gains. More specific targets were the blood and liver. A mild anemia was seen in rats together with a compensatory increase in red blood cell formation in the bone marrow. Rats also displayed dilatation of the abdominal blood vessels with inflammation of the arteries demonstrated histologically. Elevated liver weights and/or liver cell size were demonstrated in rats, mice and dogs. These liver effects were a probable reflection of increased xenobiotic metabolic activity rather than direct organ toxicity, or a combination of both effects.

An increased incidence of pulmonary tumours in male mice and of testicular interstitial cell tumours in rats were not considered to be a reflection of a potential human carcinogenicity risk. These tumours are common in these species and were not accompanied by increases in preneoplastic lesions, or a reduction in time to onset of the tumour, nor were they associated with a decreased survival rate of treated animals. In in vivo studies dimethomorph did not display genotoxic potential. In rats dimethomorph was neither a reproductive toxin nor a teratogen, and in rabbits, although maternally toxic at extreme doses, was not a teratogen.

Based on an assessment of the toxicology and the potential dietary intake of residues, it was considered there should be no adverse effects on human health from the proposed use of dimethomorph as a component of ACROBAT MZ 690 FUNGICIDE.

Residues in food

Residue data from trials conducted in Australia and overseas supported the use of dimethomorph on cucurbits, lettuce, onions and potatoes. Overall, the data indicated that there were unlikely to be detectable residues in potatoes and onions, and that residue levels in cucurbits and lettuce would not exceed the maximum residue limit (MRL) when the product is used in accordance with the recommended use pattern on the label.

Withholding periods set for the product are those determined by mancozeb. Dimethomorph does not accumulate in the fat of animals, and studies showed that most of the compound was excreted by animals unchanged.

Trade

Combination products of dimethomorph with mancozeb are registered in a number of overseas countries, including Austria, Germany, Ireland, Italy, Japan, Netherlands, Spain, Switzerland and the United Kingdom. Products based on dimethomorph alone are registered in France, Greece and Paraguay, as well as some of the countries listed above.

ACROBAT MZ 690 FUNGICIDE will not be used on any major Australian export commodities, and therefore use of the product as recommended will not result in any situation which is likely to unduly prejudice Australian trade.

Occupational health and safety

Worksafe Australia conducted a risk assessment on ACROBAT MZ 690 FUNGICIDE. Dimethomorph is not classified as a hazardous substance, but the product ACROBAT MZ 690 FUNGICIDE is a hazardous substance according to National Occupational Health and Safety Commission criteria due to the skin sensitizing properties of mancozeb, which is a hazardous substance. A re-entry period is not required, but workers are expected to follow good agricultural practice and avoid handling treated crops soon after application.

ACROBAT MZ 690 FUNGICIDE will initially be imported into Australia fully formulated and packaged. The product can be used safely if handled in accordance with the control measures prescribed on the label. Additional information is provided on the Material Safety Data Sheet for the product.

INTRODUCTION

This publication provides a summary of the data reviewed and an outline of the regulatory considerations for the proposed application of the chemical dimethomorph as a fungicide for control of various diseases of cucurbits, lettuce, onions, and potatoes. It also seeks public comment prior to the chemical product being approved for use in Australia.

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

Copies of full technical reports on occupational health and safety aspects, environmental impact, and residues in food are available from the NRA on request. They can also be viewed at the NRA Library located at the NRA's offices on Level 1, Computer Associates House, 10 National Circuit, Barton, ACT 2604.

Comments should be received by the NRA by 8 April 1997. They should be sent to:

Ms E Taverner
Agricultural Registration
NRA
PO Box 240
KINGSTON ACT 2604

FAX: (06) 272 3218

Applicant

Cyanamid Agriculture Pty Ltd has applied for registration of a fungicide product containing a new active constituent, dimethomorph, a morpholine fungicide and an existing fungicide mancozeb, a dithiocarbamate.

Product details

Dimethomorph will be marketed under the trade name ACROBAT MZ 690 FUNGICIDE as a wettable powder formulation containing 90g/kg dimethomorph and 600g/kg mancozeb.

ACROBAT MZ 690 FUNGICIDE will be imported fully formulated and packed from Germany.

Cyanamid Agriculture Pty Ltd intends to market ACROBAT MZ 690 FUNGICIDE in all States and Territories for the control of various fungal diseases of cucurbits, lettuce, onions and potatoes.

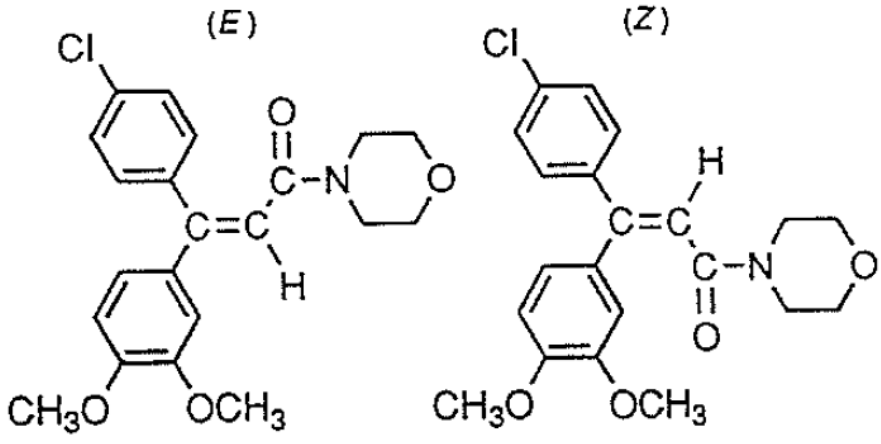
CHEMCAL PROPERTIES

Active constituent

The chemical active constituent dimethomorph is manufactured in the Netherlands and has the following properties:

Common name (ISO):	dimethomorph
Chemical name:	4-(3-(4-chlorophenyl)-3-(3,4-dimethoxyphenyl)acryloyl) morpholine
Product name:	Acrobat MZ 690 Fungicide
CAS Registry Number:	110488-70-5
Empirical formula:	$C_{21}H_{22}C1N0_4$
Molecular weight:	387.9
Physical form:	crystalline powder at ambient temperature
Colour:	colourless to grey
Odour:	odourless
Melting point for	
E/Z mixture (1:1):	125.2°C-149.2°C
Density:	1.318 (based on OECD guideline, Paris 1981)
Octanol/water partition	
coefficient K_{ow})	430($logP_{ow}$2.63) at 20°C for the E-isomer
	543($logP_{ow}$2.73) at 20°C for the Z-isomer
Vapour pressure at 25°C:	9.7 x 10^{-7} Pa for the E-isomer
	1.0 x 10^{-6} pa for the Z-isomer

Structural formula:



Formulated product

The active ingredients dimethomorph and mancozeb are formulated into wettable powder in the agricultural chemical product ACROBAT MZ 690 FUNGICIDE at the site of manufacture in Germany. The fully formulated product will be imported into Australia.

As dithiocarbamate products are date-controlled products, a shelf life is required for ACROBAT MZ 690 FUNGICIDE. Stability data provided by the applicant supported a shelf life of 2 years for the product.

AGRICULTURAL ASSESSMENT

Justification for use

ACROBAT MZ 690 FUNGICIDE is a combination of the new morpholine fungicide, dimethomorph, and the commonly used protective fungicide, mancozeb, which has been developed in this formulation in an attempt to delay the onset of fungicide resistance to dimethomorph, a potential risk when systemic products are used alone.

Phenylamide fungicides, usually in combination with mancozeb or propineb, have been widely and successfully used in Australia over the past 15 years for the control of the major Phycomycete diseases of crops such as cucurbits, grapevines, lettuce, onion, potatoes and tobacco.

Fungicide resistance in fungal pests of onions, lettuce and more recently cucurbits is becoming more widespread. There is a need for a new fungicide such as ACROBAT MZ 690 FUNGICIDE with alternative chemistry and a different mode of action but a similar disease control spectrum.

Proposed use pattern

Dimethomorph is proposed to be used in the control of various fungal diseases of cucurbits, lettuce, onions and potatoes. The product is for use by ground sprayer and has been shown when applied at 2.0 kg/ha to give good control of downy mildew, anthracnose, gummy stem blight, alternaria leaf spot and septoria spot of cucurbits; downy mildew, anthracnose and septoria leaf spot of lettuce; downy mildew, leaf blight and purple blotch of onions; and late blight and early blight of potatoes.

Registration for use on cucurbits is proposed for control of downy mildew of cucurbits in all States and Territories and for control of anthracnose, gummy stern blight, alternaria leaf spot and septoria spot in Queensland and the Northern Territory only. Use on lettuce is for control of downy mildew, anthracnose and septoria leaf spot in all States and Territories. Use on potatoes is for control of late and early blight in all States and Territories, and use on onions is for control of downy mildew in all States and Territories and purple blotch in Queensland and the Northern Territory only.

Harvest withholding periods of 7 days for cucurbits and onions, 14 days for lettuce and 49 days for potatoes have been recommended, and these appear on the ACROBAT MZ 690 FUNGICIDE label.

Evaluation of efficacy

Data from a series of field trials in Australia between 1988 and 1994 were presented, covering conditions which were suitable for moderate to severe disease development. Trials

were carried out to test the efficacy of dimethomorph against downy mildew on onions, lettuce, grapevines and cucurbits and against late blight of potatoes. The known efficacy of mancozeb against other diseases listed on the label was taken into account, and supporting argument and overseas data were used to indicate that efficacy was maintained when mancozeb was mixed with dimethomorph.

Phytotoxicity

There was no evidence of significant phytotoxicity of the formulation on target crops with the possible exception of lettuce in one Victorian trial with a: liquid formulation of 100g/L dimethomorph.

Resistance management

The label recommends that ACROBAT MZ 690 FUNGICIDE be applied as part of a regular protectant spray program when conditions favour disease development but before the disease is evident. Two consecutive sprays of ACROBAT MZ 690 FUNGICIDE 7 to 10 days apart should be followed by a fungicide from another chemical group. The label warns that no more than four ACROBAT MZ 690 FUNGICIDE sprays should be made to anyone crop as a precaution against the development of fungicide resistance. A fungicide group identification symbol and fungicide resistance warning has been included on the label of the product.

ENVIRONMENTAL ASSESSMENT

Environmental exposure

ACROBAT MZ 690 FUNGICIDE contains the technical grade active constituents dimethomorph at 90 g a.i./kg and mancozeb at 600 g a.i./kg and is proposed for use in a regular protectant spray program against various fungal diseases in cucurbits, lettuce, onions and potatoes in various States. The product is to be applied when conditions favour disease development, but before disease is evident. For all crops, the label gives directions for two consecutive sprays at 180 g a.i./ha (2.0 kg product/ha) 7-14 days (7-10 days for onions) apart before switching to a fungicide in another chemical group to avoid resistance developing in target fungi populations, with a maximum of four applications per season.

Environmental chemistry and fate

Dimethomorph will be applied by boom sprayers to vegetables, up to four times per year, to control various fungal diseases. Significant contamination of soil is likely from spray missing foliage and from run-off. Spray drift and run-off are likely to be the main means of off-site contamination.

Abiotic transformation

Dimethomorph does not hydrolyse and photolyses slowly in water with an estimated half-life of 50 to 56 days when exposed to 12 hours of natural sunlight per day. It degrades more slowly on soil surfaces with an estimated half-life of 150 days in the field. During phototransformation, the E:Z isomer ratio shifts in favour of the fungicidally active Z isomer to about 30:70.

Biotic transformation

Aerobic biodegradation half-lives in two soils ranged from 69 to 117.5 days, indicating moderate persistence. The significant amounts of radioactivity that could not be extracted from the soils (44 and 57% for the morpholine and chlorophenyl ring labels,

respectively) could not be characterised, but would presumably not be bioavailable for uptake in organisms. A greater amount of $^{14}CO_2$, was evolved for the morpholine ring (28%) than for the chlorophenyl ring (16%) labelled dimethomorph, indicating that the former is more labile. As only small amounts of polar and water soluble material were found and there was a progressive increase in unextractable material, it was concluded that dimethomorph was degraded to a metabolite which was either bound directly to soil itself, or was bound after further degradation, and that mineralisation to CO_2 occurred at least in part via the non-extractable residues. The ready biodegradability test indicated did not inhibit the growth rates of microbial populations.

Anaerobic incubation showed a more rapid initial degradation (DT50 of 5-23.9 days) followed by a significant slowing where up to 14.3% of the originally applied radioactivity was still detectable after 60 days. Two demethylated biodegradation products (with E and Z isomers of both) were found accounting for 14.8%, but in general metabolites were < 10% of applied radioactivity. Anaerobic incubation released ≤; 1 % of the radioactivity as $^{14}CO_2$, for both labelling positions. Approximately 70% of applied radioactivity was present in unextractable or bound residues at the conclusion of both experiments (60 days of inundation), and it was concluded that the mono-des methyl metabolites are likely to form di-demethyl dimethomorph, which then forms bound residues.

The biodegradation of dimethomorph was rapid in two aerobic sediment-water systems obtained from the field. Half-lives for parent compound were 2.09 and 2.94 days in the whole system with disappearance of parent from water at 7 days after treatment (DAT) with no detections in sediment at ≥:29 DAT. An unidentified metabolite peaked at 16.4% of the originally applied radioactivity in one sediment at the 61 and 105 DAT sampling times. CO_2, peaked at 21.9 and 13.8% in the two systems at the final 105 DAT sample while no organic volatiles were detected.

Mobility

Adsorption/desorption studies produced calculated Koc values of 290-566 mL/g in seven soil textures, which showed low to medium mobility. However, a soil column leaching study of the parent material (formulated in ACROBAT MZ 690 FUNGICIDE) found no residues were leached below 30 cm after the equivalent of 20 cm of water. Aged soil residue leaching studies through similar columns showed 5:3.4% of the originally applied radioactivity was found in the leachate and comprised water-soluble metabolites rather than parent compound. Greater than 47.5% of the radioactivity, of which ≤17.9% was parent, remained in the treated 5 cm layer of soil and the top 10 cm of untreated soil. Based on these studies, aged residues of dimethomorph are not expected to leach in significant quantities, even though groundwater ubiquity score values for dimethomorph indicate a potential for leaching.

Field dissipation

Moderate persistence indicated in aerobic soil incubation studies in the laboratory was also found in four field dissipation studies in soils ranging in texture from sandy loam to clay. In these studies, the dissipation half-life for dimethomorph ranged from 43.3 to 69.3 days and the ratio of isomers E:Z altered from approximately 50:50 at the start of each study to

approximately 25:75 at the end (-6 months). Low mobility in soil indicated by column leaching studies was evident in one of the field dissipation studies, where dimethomorph was not detectable (<0.005 mg a.i./kg soil) in soil samples taken at depths of 10-20 and 20-30 cm. No information was presented on metabolite formation in the field.

Accumulation in soil

Based on a worst-case scenario of a 69.3-day half-life from field dissipation studies which would result in a 2.6% annual carryover and a maximum of six applications of dimethomorph each season, approximately 28.1 g a.i./ha (equivalent to 0.014 mg a.i./kg soil in the top 15 cm) would be present in the soil after one year.

Uptake in plants

Radiolabelled residues were taken up by wheat, lettuce and carrots in lower concentrations the longer a dimethomorph-treated soil had been aged. After 29 days aging and 36 days of growth, lettuce plants contained 20.0% and 68.6% of extractable and non-extractable residues, respectively; parent compound accounted for 17.0% of the 20.0% extractable radioactivity, while 3% was unknown. In contrast, a maximum of 3.2% (≥0.8% parent) was extractable and 58.2 to 69.3% was non-extractable from the tissues of all plants after 361 days aging. The study showed that dimethomorph was taken up and translocated by these plants and likely metabolised into non-extractable residues.

Environmental toxicology

Birds

Dimethomorph was practically nontoxic to bobwhite quail and mallard duck by the single oral dose route with LD50 values greater than the highest doses tested of 2,000 mg a.i./ kg body weight. In 5-day dietary exposures with 9 days observation, both species were similarly not affected with an LC50 > 5,200 mg a.i. /kg food.

Fish

Dimethomorph when tested alone was moderately toxic to rainbow trout and bluegill sunfish with a 96-h LC50 value of 7.9 (6.0, 9.5) for trout and EC50 (lethargy) and LC50 values of 3.88 (3.37, 4.43) mg a.i.1L and 16.3 (11.1, 665) mg a./L for sunfish. Carp were less sensitive showing slight toxicity with LC50 = 18.7 (17.6, 19.7) mg a.i./L. When dimethomorph was applied in conjunction with mancozeb to rainbow trout fingerlings as the proposed ACROBAT MZ 690 FUNGICIDE, the LC50 of dimethomorph dropped to 0.043 (0.034, 0.054) mg a.i./L (with a corresponding mancozeb LC50 of 0.29 mg a.i./L) classifying these compounds as very highly and highly toxic, respectively, when applied together.

The concentrations causing 0 and 10% mortality to trout fingerlings in a 14-day chronic exposure of formulated dimethomorph/mancozeb (as ACROBAT MZ 690 FUNGICIDE or a

closely related product) were 0.017/0.11 and 0.036/0.24 mg a.i./L, respectively, confirming the classification of very highly and highly toxic, respectively. The reasons for the increased toxicity when dimethomorph and mancozeb are applied together are unclear. The toxicities of the individual E and Z isomers, while unknown, is not a serious data gap. Significant differences are not expected and the overall toxicity of a change in isomer ratio would have been accounted for during the toxicity bioassays.

Aquatic invertebrates, macrophytes and algae

A single study submitted on the acute toxicity of dimethomorph alone to *Daphnia magna* was not considered valid, and the company should provide another study of acceptable quality if future formulations contain dimethomorph alone. Mancozeb has a reported acute toxicity (48-h EC50*)* to *Daphnia magna* of 0.58-1.3 mg a.i/·L (US EPA 1996). A 48-hour static toxicity test using the proposed ACROBAT MZ 690 FUNGICIDE formulation found dimethomorph/mancozeb to be highly toxic, with an EC50 value of 0.13 (0.09, 0.19)/0.87 mg a.i/L. This value was consistent when the test was repeated and in a 21-day chronic study which found an LC50 of 0.038 (0.024, 0.055)/0.25 mg a.i./L. The NOEC and LOEC for reproduction were 0.015/0.10 and 0.046/0.31 mg a.i./L, respectively, for dimethomorph/mancozeb. Again the cause of the enhanced toxicity is unknown.

The inhibition concentration (lC50) of dimethomorph alone to the relatively insensitive freshwater green alga *Scenedesmus subspicatus chodat* was 25.3 mg a.i./L. It is noted that mancozeb (present in ACROBAT MZ 690 FUNGICIDE) has significantly higher toxicity to the green alga *Chlorella pyrenoidosa* with a 48-EC50 of 1.1 mg a.i./L (US EPA 1996).

Terrestrial invertebrates

Dimethomorph was relatively nontoxic to adult worker honey bees in oral and topical dosing experiments with LD50 > 100 µg a.i.·per bee. It is noted that mancozeb (present in ACROBAT MZ 690 FUNGICIDE) is also relatively nontoxic to bees (Tomlin 1994). The LC50 of dimethomorph to the earthworm *Eisenia foetida foetida* was greater than 1,000 mg a.i./kg soil· The predatory mite *Phytoseiulus persimilis* showed only *S.6%* mortality of nymphs when exposed to a maximum of 2 kg a.i/ha of a WP formulation of dimethomorph alone. The number of eggs laid and their hatchability did not appear to differ between treatments and controls. However, it should be noted that in a laboratory bioassay study with predatory mites from Australian vineyards, James and Rayner (1995) found zero mortality in *Typhlodromus doreenae,* but 68% and 100% mortality respectively in *Amblyseius victoriensis* mites exposed to mancozeb (Dithane is present in ACROBAT MZ 690 FUNGICIDE) at concentrations of 0.16% a.i. (field rate) and 10X that rate. The applicant has commented that the amount of mancozeb in this product is generally lower than in other products containing mancozeb and thus would not present any increased hazard in integrated pest management (IPM) programs. Beneficial arthropods such as predatory beetles, spiders and those involved in leaf litter breakdown showed no treatment-related effects and were not significantly different from controls in a field study where ≤ 20% of the applied ACROBAT MZ 690 FUNGICIDE reached the soil through the potato plant foliage.

Terrestrial plants and soil micro-organisms

Dimethomorph is presumed to be relatively nontoxic to plants as it is proposed for use on crops. However, it caused 10% mortality of coast ash saplings *(Eucalyptus sieberi)* at 23.1 mg a.i./kg soil. Studies at up to 10X the maximum rate *(*2.4/16 mg a.i./kg soil) of ACROBAT MZ 690 FUNGICIDE on soil nitrification, ammonification and respiration processes showed transitory differences of greater than 15%. The differences subsided by 91 DAT.

Environmental hazard

The environmental hazard of dimethomorph will be highest to organisms living in the vicinity where it will be applied in conjunction with mancozeb. Residues would be expected on plant surfaces, including the crop canopy, crop itself and inter-row plant cover, and on soil invertebrates exposed to spray. Surface water, uncultivated land and nearby non-target plants (e.g. trees and grasses) may be exposed through overspray, spray drift and/or run-off.

Expected environmental concentrations

In a worst-case scenario of a direct overspray of a 15 cm deep body of water with the single maximum application rate of 180 g ai/ha, the estimated environmental concentration (EEC) would be 0.12 mg a.i./L. In soil, the maximum application rate would result in an EEC of 92 µg ai./kg soil in the top 15 cm of soil with a bulk density of 1.3 g/mL.

Hazard to terrestrial organisms

Birds The EEC of dimethomorph in the diets of bob white quail and mallard duck after a single treatment at the maximum application rate were estimated as 81 and 29 mg a.i./kg food. If the maximum of six sprays per season were applied for grapes, the EEC in the birds' diets would be 474 and 177 mg a.i./ kg food, respectively, presuming a cumulative effect with no dissipation/degradation between sprays. The 5-day dietary LC50 for both species was > 5,200 mg a.i./ kg food -at least 11X and 29X higher than the EECs for quails and ducks, respectively. Thus the proposed maximum application rate of dimethomorph is not expected to pose an unacceptable hazard to these birds, as birds are unlikely to consume only contaminated food. Although no one generation chronic feeding studies were submitted, the hazard is not expected to be significant given the low toxicity exhibited in the single oral dose and 5-day dietary routes of exposure.

Earthworms. The LC50 for earthworms was found to be > 1,000 mg a.i./·kg soil which is at least 10,900X greater than the EEC in soil of 0.092 mg a.i./kg soil. Even when accounting for a maximum of six applications per season, the LC50 » EEC and the proposed use of dimethomorph is not expected to be a hazard to earthworms.

Beneficial arthropods. A similar calculation for predatory mites shows that the LD50 for dimethomorph to *Phytoseiulus persimilis* of >2 kg a.i./ha is 11X greater than the maximum application rate of dimethomorph (180 g a.i./·ha). Under a worst-case scenario of six

applications per season and 100% accumulation, this is reduced to 1.8X and a potential hazard exists. However, given that mites have a short life cycle, that much of the applied chemical does not remain on foliage and that for at least part of the spraying season some fresh plant growth is likely between spray applications, the hazard from dimethomorph is reduced.

The mancozeb present in ACROBAT MZ 690 Fungicide itself presents a potential hazard to predatory mites. Research with predatory mite species present in Australian vineyards shows that mancozeb is safe for *Typhlodromus doreenae* but is highly toxic to *Amblyseius victoriensis* (James and Rayner 1995). The applicant has commented that the amount of mancozeb in ACROBAT MZ 690 FUNGICIDE MZ 690 FUNGICIDE is generally lower than that in other products containing mancozeb and thus would not present any increased hazard in IPM programs. Environment Australia agrees with this rationale.

The abundance of beneficial arthropods was found not to be significantly different from controls in a field experiment after seven applications simulating actual use of the WP formulation of the product containing dimethomorph and mancozeb.

Soil microorganisms. The NOEC for the respiration of soil microbial organisms and the processes of nitrification and ammonification was 2.4 mg ai.1kg soil. This is 26X greater than the EEC in soil of 0.092 mg a.i./kg soil. Thus dimethomorph is not expected to be a hazard to soil microorganisms.

Hazard to aquatic organisms

Direct overspray. Data for aquatic toxicity can be used to calculate an Environmental Hazard Quotient (Q=EEC/LC50*)* for dimethomorph alone and together with mancozeb and other adjuvants in the proposed ACROBAT MZ 690 FUNGICIDE formulation. Calculated Q values for the most susceptible aquatic species tested from a single direct spray to lentic water 15 cm deep (EEC = 0.12 mg a.i./-L) show that the Q values for dimethomorph alone (rainbow trout LC50, bluegill sunfish EC50 lethargy and algae) fall in the 'no environmental risk' category. This is also the case for daphnids but must be treated with caution due to the questionable nature of the EC50 value.

However, while dimethomorph alone was moderately toxic to rainbow trout and bluegill sunfish, dimethomorph in the formulated product containing mancozeb was very highly toxic to fish and daphnids, resulting in Q values > 1 for both rainbow trout and *D*. *magna,* which would result in a presumption of unacceptable risk to aquatic organisms in the worst case. No such data are available for algae. With four spray applications per year in vegetables (and up to six proposed in grapes), there is likely to be a hazard to aquatic life from a direct overspray with the formulated product.

Surface water which could potentially be contaminated includes rivers, irrigation and drainage channels and farm dams, which could be reached by direct spraying with careless application practices. Use of suitably designed and maintained spraybooms under appropriate conditions should reduce the hazard to aquatic organisms. However, there could be a serious hazard to aquatic organisms from the possible synergism between dimethomorph and mancozeb in the

proposed formulation from a direct overspray, particularly if aerial application is allowed in the future.

Spray drift or run-off. Direct overspray from ground application, particularly repeated, is unlikely. A more likely situation in practical use of this product is contamination of surface waters by spray drift and run-off of material adsorbed to soil and organic matter particles. From this exposure, the concentration of dimethomorph in water is estimated to be approximately 10% of the direct spray amount or 12 µg/L. The Q values calculated from (i) an acute exposure for rainbow trout to a single spray of ACROBAT MZ 690 FUNGICIDE (combined toxicity of dimethomorph and mancozeb), and (ii) a chronic exposure of daphnids are both approximately 003. This fall into the 'presumption of risk that may be mitigated by restricted use' category. The risk to algae of the combined toxicity is unknown.

The risk of multiple sprays per season to fish and daphnids is not likely to be greater than that for individual sprays as studies have shown the low persistence of dimethomorph in water. The aerobic biodegradation of dimethomorph was rapid in two sediment-water systems with half-lives for parent compound of 2.09 and 2.94 days in the whole system with disappearance from water after 7 DAT with no detections in sediment at ≥29 DAT. As the label states that repeat sprays should be made at 7 to14 day intervals, no accumulation in water is expected between applications or annually.

Although no chronic hazard is expected from the proposed use, the acute effects of spray drift may still pose an unacceptable hazard to fish.

For the proposed use pattern of ACROBAT MZ 690 FUNGICIDE on cucurbits, lettuce and onions, it is expected that tractor-mounted boom sprayers producing large droplet sizes will be used which will decrease the likelihood and extent of spray drift. If the amount of spray drift were reduced to 5% and the depth of water increased to 30 cm, the Q value for fish and daphnids would be approximately 0.08, indicating acceptable risk. For these crops, the hazard from drift is expected to be acceptable. For potatoes, however, pesticides may be aerially applied which may increase drift and the possibility of direct overspray of waterways. As the estimated hazard to fish from spray drift, and especially from direct overspray, appears unacceptable, aerial application should not be allowed unless further data are presented to· demonstrate a reduction in hazard. In the interim, only ground-based spraying using equipment and practices which minimise drift should be allowed.

Desirable vegetation. Slight toxicity (10% mortality) to 8-month old *Eucalyptus sieberi* was observed when treated with an equivalent soil concentration of23.1 mg a.i./kg soil. This value is 250X greater than the EEC in soil of 0.092 mg a.i./kg soil. As the proposed use pattern for dimethomorph is unlikely to result in this high dose to non-target eucalypts (even accounting for potential accumulation), its use is not expected to be a hazard to these and other plants.

Conclusions and recommendations

Dimethomorph is a morpholine fungicide which would be applied using ground-based high or low volume spray equipment in the formulation ACROBAT MZ 690 FUNGICIDE which also contains the well-known protectant fungicide mancozeb. It is moderately persistent in aerobic

soils, does not hydrolyse and only slowly photodegrades in water and on soil surfaces. It biodegrades rapidly in aerobic water-sediment systems with half-lives of <3 days and no detections in water and sediment after 7 and 29 OAT, respectively.

The greatest concern is the high joint toxicity of dimethomorph and mancozeb to fish and daphnids. As the rapid biodegradation in water precludes chronic exposure to aquatic organisms, the acute hazard only of either a 10% spray drift or a direct overspray to fish remains unacceptable. As both these routes of exposure are more likely with aerial application, this method should not be allowed unless further data are presented to demonstrate a reduction in hazard. In the interim, only ground-based spraying using equipment and practices which minimise drift should be allowed.

PUBLIC HEALTH AND SAFETY ASSESSMENT

EVALUATION OF TOXICOLOGY

The toxicological database for dimethomorph 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 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

Dimethomorph administered orally at low dosages (10 mg/kg bw) to rats is rapidly and almost completely absorbed (>95%) and widely distributed through the organs. Excretion, following metabolism by the liver, is rapid and efficient, primarily in the bile with a lesser but still significant proportion excreted via the urine. Repeated dosing did not significantly alter the excretion patterns. After high doses of dimethomorph (500 mg/kg bw orally by gavage) in rats, absorption is limited, and a high proportion of the dimethomorph is excreted unchanged in the faeces. The pattern of metabolism and excretion is otherwise not significantly altered.

Acute studies

Dimethomorph exhibits low oral, dermal and inhalational acute toxicity. Oral LD_{50} values were 3500 mg/kg bw or greater for female rats and mice, 4300 mg/kg bw for male rats, and greater than 5000 mg/kg bw for male mice. By inhalation the LC_{50} in rats was greater than 4240 mg/m^3. The dermal LD_{50} in the rabbit was greater than 2000 mg/kg bw. In the rabbit the technical grade active constituent (TGAC) caused slight eye irritation, did not cause skin irritation on intact skin, and caused slight irritation on abraded skin. Skin sensitisation was not produced on the guinea pig.

ACROBAT MZ 690 FUNGICIDE, containing dimethomorph at 90 g/kg and mancozeb at 600 g/kg also exhibited a low oral, dermal, and inhalational toxicity consistent with the known low toxicity for mancozeb, the predominant active ingredient by weight, and the demonstrated low toxicity of dimethomorph. The oral LD_{50} value for female rats was 2254 mg/kg bw, and for males 1756 mg/kg bw. The dermal LD_{50} in the rat was greater than 2000 mg/kg bw for both sexes. The product did not cause skin irritation in the rabbit on intact skin and caused only slight eye irritation in the same species. Although Australia has no evidence of skin sensitisation by mancozeb, the product is assumed to be a skin sensitiser on the basis of a foreign agency report and until specific studies are provided.

Short-term studies

Mice treated with dimethomorph at up to 10000 ppm in their diet exhibited very few signs of toxicity. No animals died during the study and no clinical signs were observed in the animals of any treatment group. Relative liver weights were significantly increased in animals at the highest dose levels, although liver histology did not reveal any apparent pathology.

In rats treated orally with dimethomorph for four weeks at 0, 200, 290 and 380 mg/kg bw/day there were no deaths and clinical signs were minor and limited to the highest dose. Body weight gain was reduced at all treatment levels, relative liver weights were increased in females at 200 mg/kg bw/day and above, and in males at 290 mg/kg bw/day and above. Cell changes seen in the liver at 290 mg/kg bw/day and above were consistent with increased chemical metabolism activity. Evidence of irritation and inflammation was seen in the small intestine of all treated females and in males at the highest dose.

Rats were fed dimethomorph in their diet at levels equal to 0, 17, 81 and 290 mg/kg bw/day for four weeks. Two females and one male treated at 290 mg/kg bw/day died. Clinical signs were observed only in high dose animals and included: a marked reduction in weight gain in males and females, swollen abdomen, a thin appearance, hunched posture, loose faeces and pale extremities. At 290 mg/kg bw/day in both sexes, food consumption was reduced substantially, blood neutrophils were elevated 3 to 4 times control levels and serum urea nitrogen was twice control levels which may reflect altered kidney function or an increased breakdown of muscle protein. Females at this treatment level had an altered serum protein balance reflecting possible liver damage. At post mortem common findings at 290 mg/kg bw/day included stomachs distended with food, empty seminal vesicles, reduced uterine weights, and increased relative liver weights and decreased pituitary weights in both sexes. Pituitary weights were also decreased in males at 81 mg/kg bw/day.

In a study with dogs, one male and one female were fed dimethomorph in their diet at levels of 0, 750, 900, 1000 and 1200 ppm for one week at each level. A second pair of dogs were treated at 1200 ppm (37 to 47 mg/kg bw/day) for 14 days. The male dog in the first study lost weight and ate less at levels above 900 ppm. Vomiting, subdued behaviour and increased urination were observed on some occasions. The female animal exhibited no clinical signs but food intake was reduced above 1000 ppm. Both animals in the second study exhibited no clinical signs, but blood urea nitrogen was increased-reflecting a possible alteration of kidney function or an increase in the breakdown of muscle protein.

Long-term studies

Mice were treated with dimethomorph in the diet at 0, 10,100 and 1000 mg/kg bw/day for 104 weeks. A moderate but significant reduction in body weight gains during the middle of the study period was seen in males treated at 1000 mg/kg bw/day. An increased incidence of pulmonary tumours was found in male mice receiving dimethomorph but this was not statistically significant at the lowest or highest doses. This is a common tumour in mice. Its incidence was not dose related in females, was not accompanied by other significant effects in the lung in either sex, and was not associated with an increased mortality in treated animals. The incidence was not considered to be treatment related.

In a 52-week companion study in mice using 1000 mg/kg bw/day in the diet, alkaline phosphatase, an enzyme released in cases of liver damage, was elevated in both sexes at 13 weeks but not at 52 weeks. Relative liver weights were increased at 14 and also at 52 weeks. Evidence of irritation and damage to the lining of the lower small intestine was found in some animals at 14 weeks.

Rats were treated with dimethomorph at approximately 0, 10, 60 and 160 mg/kg bw/day in their diet for 104 weeks. Male groups treated with dimethomorph had a much higher survival rate than control animals. Other than a slight and intermittent reduction in body weight gain in females at 60 mg/kg bw/day, toxicity was only seen at 160 mg/kg bw/day. The main effect was a significant reduction in body weight gain. A mild anemia was observed intermittently in males and throughout most of the study period in females but disappeared at the end of the study. Increased formation of blood cells in the bone marrow consistent with the mild anaemia was, however, observed in females.

An increased incidence of dilated blood vessels and a decreased incidence of pale patches on the liver were observed in both males and females. Histology revealed a slight increase in liver size and an accumulation of a yellow brown granular pigment in the liver cells in females. Inflammation of the abdominal arteries, particularly those associated with the pancreas and intestinal connective tissue, was more common in males. In addition, a higher, but not significant, incidence of testicular interstitial (Leydig) cell adenoma occurred. However, no evidence of early onset or of progression to malignancy of this common rat tumour was observed.

Rats were treated in the diet at levels approximately equal to 0, 12, 50 and 140 mg/kg bw/day dimethomorph for 104 weeks. At the end of the study, body weight gain was reduced in males at 140 mg/kg bw/day and in females at 50 and 140 mg/kg bw/day. Ovarian cysts, pancreatic masses, enlarged lymph nodes of the intestinal connective tissue, enlarged and clearly defined lobes and dark spots in the liver, an accumulation of a yellow brown granular pigment in liver cells, and a reduction in incidences of enlargement of the pituitary glands were found in females at 140 mg/kg bw/day. In males at this dose increased incidences of dilated blood vessels in the intestinal connective tissue and cysts in the lumbar lymph nodes, and a reduction in the incidence of prominent lobulation of the liver were recorded. In both sexes the incidence of 'ground glass' foci was significantly higher at 140 mg/kg bw/day. Males, and to a lesser extent females, at this level had a significant increase in the incidence of inflamed arteries in the abdominal vessels, females displayed a significant increase in blood cell formation in sternal bone marrow; and males displayed an increased, but not significant, incidence of interstitial (Leydig cell) adenomas in the testes.

Dogs were treated for 52 weeks with dimethomorph in the diet at concentrations approximately equal to 0, 5, 15 and 45 mg/kg bw/day. Body weight gains were reduced in animals treated at 15 and 45 mg/kg bw/day. At 45 mg/kg bw/day levels of alkaline phosphatase, an enzyme released by damaged liver cells, and liver weights were elevated, and prostate weights were reduced. A slight increase in the amount of fat in the liver of males and a marginal increase in females was observed at 45 mg/kg bw/day.

Reproduction and developmental studies

In a three-generation reproduction study, rats were treated with 0, 100, 300 and 1000 ppm dimethomorph technical in their diet throughout mating, gestation and lactation. In females of the first parental generation, body weight gains were reduced at 300 and at 1000 ppm during the 100 days treatment prior to fertilisation, and food consumption at 1000 ppm was also reduced during this period. There were no treatment related malformations observed in pups.

Mated female rats were administered dimethomorph orally at dosages of 0, 20, 60 or 160 mg/kg bw/day, during the period of foetal development At 160 mg/kg bw/day body weight gain and food intake were reduced. The mean number of dead embryos was increased. Foetal malformations were low in incidence and normal for this strain of rat.

In a preliminary study, mated female rabbits were administered dimethomorph orally, at a dosage of 0, 300, 600 and 1000 mg/kg bw/day, during the period of foetal development. Animals treated at 1000 mg/kg bw/day displayed signs of toxicity such as spontaneous abortion and reduced weight gain. Reduced food and water intake were observed in some animals of all groups, but were more frequent at 1000 mg/kg bw/day. Body weight gain was slightly reduced at 300 and 600 mg/kg bw/day also. The mean number of total intrauterine deaths was greatly increased at 1000 mg/kg bw/day while foetal weight was slightly decreased at 600 mg/kg bw/day.

Mated female rabbits were administered dimethomorph orally at doses of 0, 135, 300 and 650 mg/kg bw/day during the period of foetal development. Three treatment related spontaneous abortions at 650 mg/kg bw/day were reported. The mean body weight increase at 650 mg/kg bw/day was reduced and food intake was markedly reduced. While at 300 mg/kg bw/day, lower weight gain, not associated with a reduced food intake, was reported in the early stages of the study. No treatment related foetal malformations were observed.

Genotoxicity

Dimethomorph TGAC was found not to be mutagenic in two S. *typhimurium* and two *E. coli* reverse mutation assays and in a gene mutation test in Chinese hamster V79 cells. The compound did not increase micronucleus formation in mouse erythrocytes, did not promote unscheduled DNA synthesis in male rat hepatocytes, and did not promote cell transformations in Syrian hamster embryo cells. In a series of three chromosome aberration studies in Chinese hamster V79 cells, the result in one was negative, another was positive and the third was equivocal. Taken together these studies do not indicate that dimethomorph is a mutagenic risk to humans.

PUBLIC HEALTH STANDARDS

Poisons scheduling

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

The NDPSC recommended that formulations containing dimethomorph be placed in Schedule 5 of the Standard for the Uniform Scheduling of Drugs and Poisons (SUSDP). As mancozeb is also a Schedule 5 poison, the product ACROBAT MZ 690 FUNGICIDE is a Schedule 5 poison. There are provisions for appropriate warning statements and first-aid directions on the product label.

NOEL/ADI

The most sensitive species tested was the rat with a NOEL of 6 mg/kg bw/day in a reproduction study. In order to calculate an Acceptable Daily Intake (ADI) for humans, a safety factor is applied to the NOEL in the most sensitive species. The magnitude of the safety factor is selected to account for uncertainties in extrapolation from animal data to humans; variation within the human population; the quality of the experimental data; and the nature of the potential hazards. Using a safety factor of 100, an ADI of 0.06 mg/kg bw/day was established for dimethomorph.

RESIDUES IN FOOD AND TRADE ASSESSMENT

Background

Dimethomorph, the new active constituent in ACROBAT MZ 690 FUNGICIDE, is a systemic fungicide used for the control of downy mildew on cucurbits, lettuce and onions and late and early blight on potatoes. The combination product with mancozeb is registered in a number of overseas countries, including Austria, Germany, Ireland, Italy, Japan, Netherlands, Spain, Switzerland and the United Kingdom. Products based on dimethomorph alone are registered in France, Greece and Paraguay, as well as some of the countries listed above.

Appropriate residue and metabolism studies were provided in accordance with the *Interim Requirements for the Registration of Agricultural and Veterinary Chemical Products* to support the use of dimethomorph in Australia on cucurbits, lettuce, onions and potatoes.

Residues in food commodities

Residue data from trials conducted in Australia and overseas were presented for cucurbits (rockmelons, melons, zucchini and cucumbers), lettuce, onions and potatoes.

Cucurbits

Two trials were conducted in Australia, one on zucchini and one on rockmelons. The recommended use pattern was employed in both trials, i.e. a maximum of four applications of ACROBAT MZ 690 FUNGICIDE at a rate of 180 g ai/ha, with a minimum seven-day re-treatment interval. The 1.5x and 2x treatments were also applied to rockmelons and zucchini, respectively. In the zucchini trial, maximum residues of 0.04 and 0.16 mg/kg were detected immediately after treatment at the 1x and 2x rates. Levels of dimethomorph at 7, 14, and 21 days after the final treatment were at or below the limit of determination, 0.02 mg/kg.

In the rockmelon trial, residues ranged from 0.05 -0.24 mg/kg for the Ix treatment, and 0.09 - 0.39 mg/kg for the 1.5x treatment. Maximum residues of 0.24 mg/kg were found at 14 days after the 1x treatment. Residues ranged 0.24 -0.02 mg/kg over the cucurbit group, and overseas data for cucumbers and melons did not extend the residues range established in the Australian trials. A withholding period of 7 days is necessary for mancozeb, therefore the withholding period in cucurbits for the combination product is also 7 days.

Lettuce

Data from two Australian trials were presented, for treatment at the 1 x or 2x rates, within the minimum re-treatment interval of 10 days. Residues ranged < 0.02 -0.38 mg/kg for the 1x treatment, and < 0.02 -5.58 mg/kg for the 2x treatment. In one of the overseas trials, where up to four applications of ACROBAT MZ 690 FUNGICIDE were made at rates of 1.6x and 3.3x, residues in all samples were below the limit of determination. In the other trial, following

similar trea1ments, residues ranged 0.015 - 0.83 mg/kg. As with the cucurbits, the withholding period is determined by mancozeb, therefore a 14-day withholding period is recommended.

Onions

Two trials were conducted in Australia, at rates up to 2.7x the maximum treatment, with an excessive number of applications and re-treatment intervals ranging 5 -14 days. All residues were below the limit of determination, 0.02 mg/kg. Similarly, data from overseas trials showed that following four applications of ACROBAT MZ 690 FUNGICIDE at 1.6x the recommended rate, maximum residues of 0.022 mg/kg were detected at 11 days. Overall, the residue data show there are unlikely to be detectable residues in onions when the product is used in accordance with the recommended use pattern. The withholding period for onions is 7 days, as determined by mancozeb.

Potatoes

A single trial was conducted in Australia, with data collected at 49 days after three applications of ACROBAT MZ 690 FUNGICIDE at the 1x and 2x rates, and a re-treatment interval of 7 days. Residues were below the limit of determination.

Similarly, data from numerous overseas trials, where an excessive number of applications were made at up to 8x the maximum recommended rate in Australia, showed that residues were at or below the limit of determination. Overall the data indicate that there are unlikely to be detectable residues in potatoes when the product is used in accordance with the recommended use pattern. As there is a nil withholding period for the use of mancozeb on potatoes, a withholding period of 49 days is set on the basis of the sampling interval in the Australian trial.

Metabolism studies

Metabolism studies were conducted on potatoes, grapevines and hydroponic tomato plants, using ^{14}C labelled dimethomorph to determine the extent of transport of the compound. Up to 68 and 85% of the detected residue in the potato plants and grapevines, respectively, was the parent compound.

Animal metabolism studies were conducted in rats, hens and lactating goats. The studies showed that up to 90, 88 and 90% of the administered radiolabelled dose in rats, hens and goats, respectively, was excreted. The remaining radioactivity was located in various tissues, with the greatest levels being present in the liver and kidney, followed by lower levels in the bile, fat/skin, heart, yolks and muscle. The metabolites in the hen and goat study were characterised and identified. The pattern of distribution of compounds in the hen tissues differed from that in the goats, with the major metabolite Z 67/69[‡] being found in all hen tissues. In the goat, the parent dimethomorph was the major compound found in all tissues except milk.*

The residue definition, established on the basis of the plant and animal metabolism studies is the parent dimethomorph.

_____

‡Metabolite Z 67/69, the mono-demethylated isomers of dimethomorph.

* The major metabolite in milk is a ring opened amide carboxylate form of the parent.

Descriptions of the analytical method were provided. Dimethomorph is determined directly, after extraction and solid-phase clean-up, using either GC with a PIN detector or HPLC with UV detection.

MRL Standard

The following additions to the *MRL Standard* have been recommended:

Table 1

Compound	Food	MRL(mg/kg)
Add:		
Dimethomorph		
VC 0045	Fruiting vegetables, Cucurbits	T0.5
VL 0482	Lettuce, head	T0.5
VL0483	Lettuce, leaf	T0.5
VA0385	Onion, bulb	0.05
VR 0589	Potato	*0.02

Table 3

Compound	Residue
Add:	
Dimethomorph	Sum of *E* and Z isomers of dimethomorph

Trade implications

ACROBAT MZ 690 FUNGICIDE is not used on any major Australian export commodities, and therefore use of the product as recommended, will not result in any situation which is likely to unduly prejudice Australian trade.

OCCUPATIONAL HEALTH AND SAFETY ASSESSMENT

ACROBAT MZ 690 FUNGICIDE is a wettable powder formulation containing a new active ingredient, dimethomorph, at 90 g/kg, and an existing active ingredient, mancozeb, at 600 g/kg.

Dimethomorph cannot be classified as a hazardous substance according to NOHSC criteria. However, ACROBAT MZ 690 FUNGICIDE is determined to be hazardous based on the skin sensitizing properties of mancozeb, which is a hazardous substance.

Dimethomorph is manufactured in the Netherlands. ACROBAT MZ 690 FUNGICIDE MZ 690 Fungicide is a greyish free flowing· odourless powder. It is formulated and packed in Germany and imported to Australia ready for dilution and use. The product is packaged in 5 kg cartons (containing 10 x 500 g water soluble measure packs) and in a 10 kg sale pack contained in a multiwall paper bag.

Manufacture, formulation, transport, storage and retailing

Australian workers will only be involved in transport, storage and retailing of the product. These workers could only come in contact with ACROBAT MZ 690 FUNGICIDE if the packaging were accidentally breached. The Safe Handling Information in the Material Safety Data Sheet (MSDS) is adequate to enable workers to safely handle spills.

End use

The product is diluted with water prior to application. Monsoon wetting agent is added at 30 mL/100 L and tank mixed with constant agitation using between 250 and 1000 L/ha water. The product is applied by high volume boom spray equipment. Small scale operators may apply the product using knapsack spray equipment. Intermittent application of the product throughout the year can occur as the crops may be planted on more than one occasion in one year, or some of the crops may be planted on a rotational basis. The concentration of dimethomorph in the prepared spray varies from 0.018% to 0.072% depending on the particular crop sprayed and selected spray volume.

Agricultural workers can come in contact with the product when opening containers, preparing spray, using prepared spray, cleaning up spills and equipment. They may also come into contact with the products when re-entering treated crops, harvesting and handling treated crops after harvest. The main routes of exposure are via the skill and respiratory routes. Of these, skin contamination is the more likely. Inhalation of spray should not be significant under field conditions because of the low toxicity of dimethomorph, its high dilution in the product, and the dissipation of spray residues in the air.

Worker exposure under Australian conditions has been estimated using the Predictive Operator Exposure Model (POEM). Control measures have been assigned to minimise the risk of health effects following short-term and repeated use of the product.

Safety directions have been included on the product label. Workers opening the container and using the prepared spray should wear cotton overalls buttoned to the neck and wrist, a washable hat and elbow length PVC gloves.

The MSDS for the product contains adequate information for routine use of ACROBAT MZ 690 FUNGICIDE.

Entry into treated areas or handling treated crops

According to the Environmental Assessment Report, dimethomorph is moderately persistent in sunlight (half-life 69 to 117 days) and under field conditions. Dimethomorph is not readily biodegradable. No residual data is available on dimethomorph. Because of the low toxicity of dimethomorph, Worksafe Australia does not recommend any restriction on re-entering treated areas. However, workers should follow good agricultural practice and avoid handling treated crops soon after application.

Worker exposure during harvest and when handling harvested crop should not be of occupational health and safety concern, considering the relatively short withholding period for the proposed uses.

Recommendations for safe use

End users should follow the instructions and safety directions on the product label. When opening containers and preparing the spray, they should wear cotton overalls buttoned to the neck and wrist [AS 3765-1990 -Clothing for Protection Against Hazardous Chemicals], a washable hat and elbow-length PVC gloves [AS 2161-1978-Industrial Safety Gloves and Mittens (excluding Electrical and Medical Gloves)].

On the basis of this assessment, no occupational health and safety standards, such as Health Surveillance or Exposure Standard, are considered necessary for dimethomorph.

Worksafe Australia has not recommended a restricted entry statement.

GLOSSARY OF TERMS

Active constituent	The component of a treatment which is responsible for its biological effect.
Acute toxicity	Immediately measurable effects of a toxin on an organism.
Denatured	Broken down.
Depuration	Cleansing, purification.
Detritus	Rotting vegetable material.
Diploid	Having two sets of chromosomes
DNA	Deoxyribonucleic acid the generic component of the chromosomes which support gene sequences.
Gene	A length of the DNA which holds the base sequences that code for the formation of a polypeptide chain (protein).
Groundwater ubiquity score	A measure of whether a compound is likely to leach through soil into groundwater.
IC_{50}	Inhibition concentration where 50% of (algal) cell growth is inhibited.
IPM	Integrated Pest Management. The combination of chemical and biological aspects of pest control to achieve pest management.
LC_{50}	The concentration of a substance that produces death in 50 per cent of a population of experimental organisms within a specified period. It is usually expressed as milligrams per litre (mg/L) or milligrams per kilogram (mg/kg) as a concentration in food, water or air**.**
LD_{50}	The dose of a substance that produces death in 50 percent of a population of experimental organisms within a specified period. It is usually expressed as milligrams per kilogram (mg/kg) of body weight.
Lentic water	Still water.
Photolysis	Breakdown caused by light.
ppm	Parts per million.
Pomace	Pulpy residue from apples or other fruit after crushing and pressing
Protease	Enzymes which break down proteins.
Proteolysis	The process in which proteins chains are lysed (cut) as part of their digestion.
Schedule	The category into which a chemical is placed according to its human toxicity.

SUGGESTED FURTHER READING

Felton, J.C., Oomen, P.A. & Stevenson, J.H. 1986, 'Toxicity and hazard of pesticides to honeybees: harmonisation of test methods', *Bee World,* vol. 67, no. 3, pp. 114-24.

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

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

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, 'Code of Practice for Labelling Agricultural Chemical Products', NRA, Canberra (draft).

Tomlin, C. (ed) 1994, *The Pesticide Manual,* 10th edn, British Crop Protection Council, Surrey, UK and The Royal Society of Chemistry, Cambridge, UK.

Urban, DJ. & Cook, N.J 1986, *Hazard Evaluation Division Standard Evaluation Procedure: Ecological Risk Assessment,* EPA 540/9-85-001, Office of Pesticide Programs, United States Environmental Protection Agency, Washington, D.C.

APPENDIX 1
DRAFT LABEL

CAUTION

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

ACROBAT* MZ 690 Fungicide

Active Constituent: 90g/kg DIMETHOMORPH
600g/kg MANCOZEB

GROUP	X	Y	FUNGICIDES

For the control of various diseases of cucurbits, lettuce, onions and potatoes as per the DIRECTIONS FOR USE table

CYANAMID

CYANAMID AGRICULTURE PTY. LIMITED
5 Gibbon Road, Baulkham Hills NSW 2153

5 kg PRIMARY PACK
CONTAINS 10 x 500g WATER SOLUBLE MEASURE PACKS WHICH IT IS ILLEGAL TO SELL SEPARATELY

* Registered trademark of American Cyanamid Company.

CAUTION

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

ACROBAT* MZ 690 Fungicide

Active Constituent: 90g/kg DIMETHOMORPH
600g/kg MANCOZEB

500g NOT TO BE SOLD SEPARATELY.
BEFORE USE, READ ALL DIRECTIONS ON OUTER PACK.
WATER SOLUBLE PACKAGING. KEEP DRY.

*Registered trademark of American Cyanamid Company.

DIRECTIONS FOR USE

CROP	DISEASE	STATE	DOSE	WHP	CRITICAL COMMENTS
Cucurbits	Downy mildew (Pseudoperonospora cubensis)	All states	2.0kg/ha	7 days	Maintain a regular protectant spray programme. Apply ACROBAT MZ when conditions favour disease development but before the disease is evident. Apply two consecutive sprays of ACROBAT MZ, 7 to 10 days apart, then change to a fungicide from another chemical group. Use the shorter interval when conditions favouring infection are creating a high risk. Add MONSOON wetting agent at 30mL/100L Do NOT apply more than 4 ACROBAT MZ sprays to each crop as a precaution against development of disease resistance**.**
	Anthracnose (Colletotrichum spp.), gummy stem blight *(Didymella bryoniae),* Alternaria leaf spot *(Alternaria spp.),* Septoria spot (pumpkin) *(Septoria spp.)*	Qld only & NT			
Lettuce	Downy mildew *(Bremia lactucae),* Anthracnose ***(****Marssonina panattoniana****),*** Septoria leaf spot *(Septoria spp.)*	All States	2.0kg/ha	14 days	Maintain a regular protectant spray programme. Apply when conditions favour disease development but before the disease is evident Apply two consecutive sprays of ACROBAT MZ, 7 to 10 days apart then change to a fungicide from another chemical group. Use the shorter interval when conditions favouring infection are creating a high risk. Apply in 250 to 500L of water per hectare. Add MONSOON wetting agent at 30mL/100L. Do NOT apply more than 4 sprays of ACROBAT MZ to each crop as a precaution against development of disease resistance.

CROP	DISEASE	STATE	DOSE	WHP	CRITICAL COMMENTS
Onions	Downy mildew *(Peronospora destructor),* leaf blight	All states	2.0kg/ha	7 days	Maintain a regular protectant spray programme. Apply when conditions favour disease development but before the

	Purple blotch *(Alternaria porri)*	Qld only & NT			disease is evident. Apply two consecutive sprays of ACROBAT MZ, 7 to 14 days apart, then change to a fungicide from another chemical group. Use the shorter interval when conditions favouring infection are creating a high risk. Apply in 250 to 500L of water per hectare. Add MONSOON wetting agent at 30mL/100L. Do NOT apply more than 4 sprays of ACROBAT MZ to each crop as a precaution against development of disease resistance.
Potatoes	Late blight *(Phytophthora infestans),* early blight *(Alternaria solani)*	All states	2.0Kg/ha	-	Maintain a regular protectant spray programme. Apply on a protectant schedule at 7 to 10 day intervals when conditions favour disease development but before the disease is evident. Use the shorter spray interval when conditions for disease development are severe. Add MONSOON wetting agent at 30mL/100L. Apply ACROBAT MZ in 250 to 500 litres of water per hectare. Do NOT apply more than 4 ACROBAT MZ sprays to each crop as a precaution against development of disease resistance.

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

WITHOLDING PERIODS:

CUCURBITS, ONIONS: DO NOT APPLY LATER 1HAN7DAYS BEFORE HARVEST.

LETTUCE: DO NOT APPLY LATER 1HAN 14 DAYS BEFORE HARVEST.

POTATOES: DO NOT APPLY LATER 1HAN 49 DAYS BEFORE HARVEST.

GENERAL INSTRUCTIONS:

FUNGICIDE RESISTANCE WARNING

GROUP	X	Y	FUNGICIDES

ACROBAT MZ 690 Fungicide is a combination of a Group X and a Group Y fungicide. For fungicide resistance management, ACROBAT MZ 690 is both a Group X and a Group Y fungicide.

Some naturally occurring individual fungi resistant to ACROBAT MZ and other Group Y fungicides containing mancozeb may exist through normal genetic variability in any fungal population. The resistant individuals can eventually dominate the fungal population if these fungicides are used repeatedly. These resistant fungi may not be controlled by ACROBAT MZ and other Group Y fungicides containing mancozeb, thus resulting in a reduction in efficacy and possible yield loss.

Since the occurrence of resistant fungi is difficult to detect prior to use, Cyanamid Agriculture Pty. Limited accepts no liability for any losses that may result from the failure of ACROBAT MZ 690 to control resistant fungi.

This product combines the locally systemic, translaminar properties of dimethomorph with the protective properties of mancozeb. It should always be used as part of a protective spray programme and applied before disease symptoms appear. To prevent or delay the development of strains of disease fungi resistant to dimethomorph, it is recommended that this product is used in spray programmes including fungicides with different modes of action. Refer to the CRITICAL COMMENTS section of this label. Consult a Cyanamid representative for further information if required.

MIXING

Half fill the spray vat and commence agitation. Add the required number of water soluble bags and allow them to disperse. Add the remainder of the water with agitation running. Add wetting agent, if required, when spray tank is full. Ensure thorough mixing and constant agitation to keep the product in suspension.

APPLICATION:

Ensure thorough coverage of plants.

Do NOT apply by aircraft.

COMPATIBILITY:

ACROBAT MZ can be tank-mixed with MVP* Bio-encapsulated Insecticide, CYBOUT® Biological Insecticide, Dipel* Forte, Lorsban* EC, Kocide* or DELAN® Fungicide.

Avoid mixing with strongly alkaline or acidic materials.

PROTECTION OF WILDLIFE, FISH, CRUSTACEANS AND ENVIRONMENT:

Highly toxic to fish and other aquatic organisms. Do NOT contaminate ponds, dams, streams, waterways or drains with the chemical or used containers.

Do NOT apply under meteorological conditions or from spraying equipment which could be expected to cause spray to drift onto nearby susceptible plants, adjacent crops, crop lands or pastures.

STORAGE AND DISPOSAL:

Store in the closed original container in a dry, well-ventilated area, as cool as possible. Do NOT store for prolonged period in direct sunlight.

Ensure that water soluble bags are kept in sealed moisture-proof original containers.

Puncture, shred and 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.

SAFETY DIRECTIONS:

Harmful if swallowed. Will irritate the eyes. Avoid contact with the eyes. Repeated exposure may cause allergic disorders. When opening the container and using the prepared spray, wear cotton overalls buttoned to the neck and wrist and a washable hat and elbow-length PVC gloves. Wash hands after use. After each day's use, wash gloves and contaminated clothing.

FIRST AID:

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

MSDS:

Additional information is listed in the Material Safety Data Sheet.

WARRANTY:

This product is designed only to be used in accordance with the label directions which reflect the opinion of experts based on field use and tests. If it is so used, Cyanamid Agriculture Pty. Limited warrants its effectiveness, but takes no responsibility whatsoever for the consequences of the user failing to follow these directions exactly.

* Registered trademarks

THIS PRODUCT IS NOT CONSIDERED TO BE A DANGEROUS GOOD UNDER THE AUSTRALIAN CODE FOR THE TRANSPORT OF DANGEROUS GOODS BY ROAD AND RAIL

FOR SPECIALIST
ADVICE IN AN
EMERGENCY ONLY

PHONE
1 800 033 111

TOLL FREE – ALLHOURS-
AUSTRALIA W1DE

Product No:

Batch No:

Expiry Date:

NRA Approval No:

AS 1/97