Public Release Summary
on

Evaluation of the new active

SPIROTETRAMAT

in the product

MOVENTO 240 SC INSECTICIDE

Australian Pesticides and Veterinary Medicines Authority

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FOREWORD

The Australian Pesticides and Veterinary Medicines Authority (APVMA) 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 APVMA works in close cooperation with advisory agencies, including the Department of Health and Aging (Office of Chemical Safety and Environmental Health), Department of the Environment, Water, Heritage and the Arts (Chemical Risk Assessment Section), and State departments of agriculture and environment.

The APVMA 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 APVMA 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 APVMA's Manual of Requirements and Guidelines - *The Manual of Requirements and Guidelines - MORAG for Agricultural and Veterinary Chemicals [Ag MORAG & Vet MORAG]*.

This Public Release Summary is intended as a brief overview of the assessment that has been completed by the APVMA 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 APVMA. Alternatively, the reports can be viewed at the APVMA Library, 18 Wormald Street, Symonston, ACT.

The APVMA welcomes comment on the usefulness of this publication and suggestions for further improvement. Comments should be submitted to the Pesticides Program Manager, Australian Pesticides and Veterinary Medicines Authority, PO Box 8162, Kingston ACT 2604.

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LIST OF ABBREVIATIONS AND ACRONYMS

ABBREVIATIONS

Time

d	Day
h	Hour
Min	Minute
Mo	Month
Wk	Week
S	Second
Yr	Year

Length

cm	Centimetre
M	Metre
µm	Micrometre
mm	Millimetre
Nm	Nanometre

Volume/Area

A	acre
ha	hectare
vmd	volume median diameter
µL	Microlitre
L	Litre
mL	Millilitre

Weight

bw	Body weight
g	Gram
kg	Kilogram
µg	Microgram
mg	Milligram
ng	Nanogram
wt	Weight

Dosing

id	Intradermal
im	Intramuscular
inh	Inhalation
ip	Intraperitoneal
iv	Intravenous
po	Oral
sc	Subcutaneous
mg/kg bw/day	mg/kg bodyweight/day

Concentration

m	Molar
ppb	Parts per billion
ppm	Parts per million

Clinical chemistry, haematology, toxicology

A/G	Albumin/globulin ratio
ALT	Alanine aminotransferase (SGPT)
AP	Alkaline phosphatase
AST	Aspartate aminotransferase (SGOT)
AUC	Area under curve
BUN	Blood urea nitrogen
ChE	Cholinesterase
CHO/HGPRT	Chinese hamster ovary/hypoxanthin-guanine-phosphoribosyl transferase (assay)
CPK	Creatine phosphatase (phosphokinase)
GGT	Gamma-glutamyl transferase
Hb	Haemoglobin
Hct	Haematocrit
LDH	Lactate dehydrogenase
LH	Luteinising hormone
MCH	Mean corpuscular haemoglobin
MCHC	Mean corpuscular haemoglobin concentration
MCV	Mean corpuscular volume
NTE	Neurotoxic target esterase
PBPK	Pharmacokinetic
PCV	Packed cell volume (Haematocrit)
PT	Prothrombin time
RBC	Red blood cell/erythrocyte
T_3	Triiodothyroxine
T_4	Thyroxine
TSH	Thyroid stimulating hormone (thyrotropin)
WBC	White blood cell/leucocyte
WBC-DC	White blood cells – differential count

Anatomy

CNS	Central nervous system
GIT	Gastro-intestinal tract
in vitro	outside the living body and in an artificial environment
in vivo	inside the living body of a plant or animal

Chemistry

^{14}C	Carbon 14 or radiocarbon
GC	Gas chromatography
GLC	Gas liquid chromatography
HPLC	High Pressure Liquid Chromatography *or* High Performance Liquid Chromatography
LC-MS/MS	Liquid chromatography, mass spectroscopy
MS	Mass spectrometry
RIA	Radioimmunoassay
TGAC	Technical grade active constituent
TLC	Thin layer chromatography

Environment

AR	Applied Radioactivity
DFR kinetics	
DFOP kinetics	Double First Order in Parallel kinetics
E_bC_{50}	Concentration at which algal biomass growth is inhibited by 50%
FOMC	First-Order Multi Compartment
K_d	Linear adsorption constant
K_F	Freundlich adsorption coefficient
K_{FOC}	Linear adsorption constant
K_{OC}	Organic carbon partitioning coefficient
Log P_{ow}	Partition Coefficient
LR_{50}	Lethal rate (Application rate at which 50% mortality is observed)
NER	Non-Extractable Radioactivity
SFO kinetics	Simple First-Order kinetics
SFO-RB kinetics	Simple First-Order Reverse Binding kinetics

Residues

AD	Administered dose
BBCH scale	Biologische Bundesanstalt, Bundessortenamt and Chemical industry scale
Codex	Codex Alimentarius Commission
CXLs	Codex Maximum Residue Limits
HR	Highest Residue
RACs	Raw Agricultural Commodities

Terminology

ac	Active constituent
ADI	Acceptable Daily Intake
ai	Active ingredient
AOEL	Acceptable Operator Exposure Level
ARfD	Acute Reference Dose
bw	bodyweight
DAT	Days After Treatment
DFR	Dislodgeable Foliar Residue
DT_{50}	Time taken for 50% of the concentration to dissipate
DT_{90}	Time taken for 90% of the concentration to dissipate
E_bC_{50}	Concentration at which the biomass of 50% of the test population is impacted
EC_{50}	Concentration at which 50% of the test population are immobilised
EEC	Estimated Environmental Concentration
E_rC_{50}	Concentration at which the rate of growth of 50% of the test population is impacted
Fo	Original parent generation
GCP	Good Clinical Practice
GLP	Good Laboratory Practice
GVP	Good Veterinary Practice
IPM	Integrated Pest Management
K_{ow}logP	Partition Coefficient

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
LOEL	Lowest Observed Effect Level
LOD	Limit of Detection – level at which residues can be detected
LOQ	Limit of Quantitation – level at which residues can be quantified
MRL	Maximum Residue Limit or Level
MSDS	Material Safety Data Sheet
NEDI	National Estimated Daily Intake
NESTI	National Estimated Short Term Intake
NOEL	No Observed Effect Level
NOAEL	No Observed Adverse Effect Level
NOEC/NOEL	No Observable Effect Concentration/Level
OP	Organophosphorus pesticide
OC	Organic Carbon
OM	Organic Matter
PHED	Pesticide Handler Exposure Database
POEM	Predictive Operator Exposure Model
PPE	Personal Protective Equipment
Q-value	Quotient-value
SC	Suspension Concentrate
TC	Transfer Co-efficients
TRR	Total Radioactive Residues
T-Value	A value used to determine the First Aid Instructions for chemical products that contain two or more poisons
WG	Water Dispersible Granule
WHP	Withholding Period

Organisations & publications

AGCS	Advisory Group on Chemical Safety
BBA	Biologische Bundesanalstalt fur Land – und forstwirschaft
CAC	Codex Alimentarius Commission
DEWHA	Department of the Environment, Water, Heritage and the Arts
ECETOC	European Chemical Industry Ecology and Toxicology Centre
FAO	Food and Agriculture Organisation of the UN
FAISD	First Aid Instructions & Safety Directions
IARC	International Agency for Research on Cancer
IPCS	International Programme on Chemical Safety
JECFA	FAO/WHO Joint Expert Committee on Food Additives
JMPR	Joint Meeting on Pesticide Residues
NCI	National Cancer Institute
NDPSC	National Drugs and Poisons Scheduling Committee
NHMRC	National Health and Medical Research Council
NOHSC	National Occupational Health & Safety Commission
NTP	National Toxicology Program
OECD	Organisation for Economic Co-operation and Development
OCS	Office of Chemical Safety
SUSDP	Standard for the Uniform Scheduling of Drugs and Poisons
TGA	Therapeutic Goods Administration
US EPA	United States Environmental Protection Agency
WHO	World Health Organisation

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INTRODUCTION

This publication provides a summary of the data reviewed and an outline of the regulatory considerations for the proposed registration of *MOVENTO 240 SC INSECTICIDE,* which contains the new active constituent spirotetramat. The product is proposed` for use as foliar insecticides for the control of silverleaf whitefly (*Bemisia tabaci* Biotype B) in broccoli, broccolini, Brussels sprouts, cabbage and cauliflower.

The purpose of this summary is to inform the public of the proposed registrations and invite comment on this proposal.

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

Copies of full technical evaluation reports on spirotetramat, covering toxicology, occupational health and safety aspects, residues in food and environmental aspects are available from the APVMA on request (see order form on last page of this document). They can also be viewed at the APVMA library located at the APVMA offices, 18 Wormald St, Symonston, ACT 2609.

Written comments should be received by the APVMA by 1 June 2009. They should be addressed to:

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Applicant

Bayer CropScience Pty Ltd

Details of Product

It is proposed to register *MOVENTO 240 SC INSECTICIDE (MOVENTO)* containing spirotetramat at 240g/L as a suspension concentrate formulation. *MOVENTO* will be imported fully formulated and packaged in 1L, 2.5L, 5L and 10L containers.

MOVENTO is a new insecticide and is the first member of a new chemical class, the cyclic ketoenoles. It is a tetramic acid derivative with a novel mode of action that interferes with lipid biosynthesis, leading to the death of immature stages of the target insect two to ten days after application. Spirotetramat inhibits acetyl CoA carboxylase, a key enzyme in fatty acid biosynthesis. The active constituent is active against a wide spectrum of sucking insects, including aphids, scales (soft and armoured), mealybugs, whiteflies, psyllids and selected thrip species.

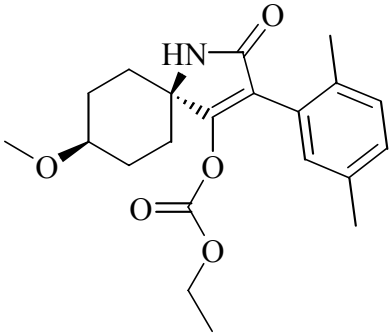
MOVENTO is proposed for use in Australia as a foliar insecticide for the control of silverleaf whitefly in broccoli, broccolini, Brussles sprouts, cabbage and cauliflower.

Spirotetramat is currently registered overseas in the United States of America, and Canada as both a 240g/L suspension concentrate and as a 100g/L oil dispersion. The 240g/L suspension concentrate is also registered in New Zealand. There are a number of other countries that have granted registration to the 100g/L oil dispersion. These registrations are on a number of different crops at a number of different rates.

CHEMISTRY AND MANUFACTURE

Active Constituent

The chemical active constituent has the following properties:

Common Name:	Spirotetramet
Chemical Name (IUPAC):	*cis*-4-(Ethoxycarbonyloxy)-8-methoxy-3-(2,5-xylyl)-1-azaspiro[4.5]dec-3-en-2-one
CA Name:	*cis*-3-(2,5-Dimethylphenyl)-8-methoxy-2-oxo-1-azaspiro[4.5]dec-3-en-4-yl ethyl carbonate
CAS Registry Number:	203313-25-1
Empirical Formula:	$C_{21}H_{27}NO_5$
Molecular Weight:	373.45
Physical form:	Powder
Colour:	Light beige
Melting Point:	142 °C
Density:	1.23 g/cm^3
Octanol/water partition coefficient:	log P_{OW} = 2.51 (at pH 7)
Vapour pressure at 25 °C:	5.6×10^{-9} mm Hg
Chemical Structure:	
Chemical Family:	Cyclic ketoenol
Chemical Type:	Insecticide
Mode of Action:	Lipid biosynthesis inhibitor

Summary of the APVMA's Evaluation of Spirotetramet Active Constituent

The Chemistry Section has evaluated the chemistry aspects of spirotetramet active constituent (manufacturing process, quality control procedures, batch analysis results and analytical methods) and found them to be acceptable.

Spirotetramet is a new active constituent and there is no compendial specification available. On the basis of the data provided, the active constituent spirotetramet has been approved (approval number 61876) and the following APVMA Standard:

Active constituent	**Minimum content**
Spirotetramet	Not less than 960 g/kg

Other characteristics of spirotetramat (toxicology, environmental fate etc) are covered in subsequent sections of this Public Release Summary.

Formulated Product

Distinguishing name:	Movento 240 SC Insecticide
Formulation type:	Suspension Concentrate (SC)
Active constituent concentration:	240 g/L

Physical and Chemical Properties of the Product

Physical state:	Suspension
Colour:	White
Odour:	Aromatic
Specific gravity:	1.075 at 25 °C
Acidity, alkalinity or pH value:	4-5 (neat)
Storage stability:	Stable for at least 2 years when stored under ambient conditions.

Summary of the APVMA's Evaluation of Movento 240 SC Insecticide

The Chemistry Section has evaluated the chemistry aspects of Movento 240 SC Insecticide (manufacturing process, quality control procedures, batch analysis results, analytical methods, storage stability, and specifications for containers for the product) and found them to be acceptable.

TOXICOLOGICAL ASSESSMENT

The toxicological database for spirotetramat, 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 that are high compared with likely human exposures. The use of high doses increases the likelihood that potentially significant toxic effects will be identified. Findings of adverse effects in any one species do not necessarily indicate such effects might be generated in humans. From a conservative risk assessment perspective however, adverse findings in animal species are assumed to represent potential effects in humans, unless convincing evidence of species specificity is available. Where possible, considerations of the species specific mechanisms of adverse reactions weigh heavily in the extrapolation of animal data to likely human hazard. Equally, consideration of the risks to human health must take into account the likely human exposure levels compared with those, usually many times higher, which produce effects in animal studies. Toxicity tests should also indicate dose levels at which the specific toxic effects are unlikely to occur. Such dose levels as the No-Observable-Effect-Level (NOEL) are used to develop acceptable limits for dietary or other intakes (ADI and ARfD) at which no adverse health effects in humans would be expected.

METABOLISM AND TOXICOKINETICS ASSESSMENT

The disposition of spirotetramat was investigated in three *in vivo* and one *in vitro* studies. Gastrointestinal absorption of spirotetramat was rapid following oral administration to male and female rats at a single dose of 2 or 100 mg/kg bw or repeated doses of 2 mg/kg bw for 14 days. The absorption rate in all tests was between 89 and 98% of the total recovered radioactivity, based upon recovery from the urine and carcass (without the gastrointestinal tract). No significant differences in the absorption rate were observed among any of the dose groups. The absorption rate in the single low dose test was 95% for male rats and 96% for female rats. The maximum of plasma concentration was reached for all dose groups within 0.09 to 2.03 hours after administration (values calculated by pharmacokinetic modelling). The radioactivity concentrations in plasma declined steadily by several orders of magnitude within 48 hours for all dose groups. Radioactivity in tissues and organs at the 48-hour termination were very low (<0.2% and below the limit of detection for some organs/tissues). Urinary excretion was very rapid (essentially complete in 24 hrs) and was the major excretion route at these doses. Faecal excretion accounted for 2-11% of the dose in male and female rats. The excretion behavior was similar for all dose groups.

Spirotetramat (BYI 08330) was completely metabolized by the rat in this study; no parent compound was detected in the excreta. Identified metabolites accounted for 87-95% of the administered dose. Only very minor metabolites (<0.7% of the dose) were not identified. The main metabolic reaction was cleavage of the ester group which resulted in the formation of the primary and most predominant metabolite BYI 08330-enol (53-87% of the administered dose). All other identified metabolites could be derived from the enol intermediate. The second prominent metabolic transformation was oxidative demethylation of the 8-methoxy group to BYI 08330-desmethyl-enol (5-37% of the administered dose). Oxidation of the azaspiro moiety to BYI 08330-ketohydroxy and BYI 08330-desmethyl-ketohydroxy were detected as minor pathways. Other minor metabolic transformations were conjugation of the enol with glucuronic acid to BYI 08330-enol-GA and oxidation of the aromatic methyl group of the enol metabolite to BYI 08330-enol-alcohol. A sex-related difference was observed in metabolism in this study with male rats showing much higher rates of demethylation to BYI 08330-desmethyl-enol compared to female rats. Similar results were obtained when male and female rats were administered a single dose of 3 mg/kg bw in another disposition study using quantitative whole body autoradiography. The highest equivalent concentrations were observed in the liver, kidney, and blood in that study.

Absorption in male rats administered a single dose of 1000 mg/kg bw spirotetramat was much lower with only 27% of the dose excreted in the urine after 24 hours. Excretion was also distinctively less than for lower-dose animals, and radioactivity in plasma was slightly higher than in liver and kidney. These findings were consistent with saturation of cellular transport mechanisms. In addition, decline of tissue radioactivity was minimal from 1 h to 8 h post dose and increased only slightly at 24 hours. The metabolism profile was qualitatively similar to that of the lower doses; however, BYI 08330-desmethyl-enol occurred at lower levels at 1000 mg/kg bw, and this may be a reflection of the decreased absorption at this dose. Similar to the low dose groups, BYI 08330-desmethyl-enol levels were greater in urine than in plasma and organs. The highest percentage of BYI 08330-desmethyl-enol was detected in liver and kidney. Results of this study indicate that saturation of active transport mechanisms occurs at a dose of 1000 mg/kg but not 2 mg/kg. This results in decreased excretion via urine and faeces and a potential for accumulation of BYI 08330 related residues in the body following repeated high doses. The results of pharmacologically based pharmacokinetic (PBPK) simulations supported this conclusion and suggested that repeated daily doses of ≥300 mg spirotetramat/kg bw lead to non-linear elimination kinetics, resulting in a high body burden in multiple-dose toxicological studies. This assumes, however, that spirotetramat enters the systemic circulation as the metabolite BYI 08330-enol.

In a comparative in vitro metabolism study using hepatocytes from male rats, mice, and humans, differences in the proportions of several down-stream metabolites were observed; however, BYI 08330-enol was the first and most prominent metabolite and accounted for 66-100% of all metabolites across species.

Acute Studies

Spirotetramat technical demonstrated moderate to low acute toxicity via the oral (LD_{50}>2000 mg/kg bw), dermal (LD_{50}>2000 mg/kg bw), and inhalation (LC_{50} >4183 mg/m^3) routes. Spirotetramat is non-irritating to the skin, although it is an irritant to the eyes (severe) and exhibits a skin-sensitization potential under the conditions of the guinea pig maximization test and the local lymph node assay, but not the Buehler patch test. The sensitization potential of spirotetramat was supported by two cases of Type IV hypersensitivity that were reported in spirotetramat manufacturing plant personnel.

The product, MOVENTO® 240 SC Insecticide containing 240 g/L spirotetramat, has low acute toxicity to the rat by the oral (LD_{50}: >2000 mg/kg bw; females tested only), dermal (LD_{50}: >4000 mg/kg bw) and inhalation (LC_{50}: >3013 mg/m^3 air) routes. The product is non-irritating to the skin but it is a slight irritant to eyes in rabbits. It is a skin-sensitiser in guinea pigs however its ready to use dilution is not (Buehler Patch Tests).

Short term toxicity

The insecticidal mode of action (lipid biosynthesis inhibition) was not reflected in the results of the short-term toxicological studies in rodents and dogs. Rats, mice, and dogs did not exhibit changes in plasma lipid parameters such as plasma triglycerides and plasma cholesterol.

The thyroid and thymus glands were target organs in a 90-day feeding study with spirotetramat in dogs. Statistically significant declines in circulating thyroid hormones (T4 and/or T3) at ≥1200 ppm (32 mg/kg bw/day) were observed. However, correlative changes in thyroid weight, thyroid histopathology, or thyroid stimulating hormone (TSH) were not observed in either sex. The NOAEL was considered to be 300 ppm, equivalent to 9 mg/kg bw/d in males and 10 mg/kg bw/d in females.

The thymus, thyroid, and brain were target organs following one-year oral exposure of dogs to spirotetramat. Thymus involution and brain dilation with dose-related severity were

observed in males at ≥600 ppm (20 mg/kg bw/day), while axonal degeneration in the hypothalamus was observed in one female at 1800 ppm (48 mg/kg bw/day). Brain dilation was observed in one female at the mid dose (600 ppm) also, however, it was not observed at the high dose (1800 ppm). Both sexes showed statistically significant compound related decreases in circulating thyroid hormone T4 at 600 and 1800 ppm and for males also of T3 at 1800 ppm. Reduction in thyroid follicle size, a possible indication of a reduced amount of colloid in the organ, was observed in 1800-ppm males (55 mg/kg bw/day) only. Correlative changes in thyroid weight or thyroid stimulating hormone (TSH) were not observed in either sex. Clinical signs of neurotoxicity (dehydration, swelling, decreased activity and reactivity, seizures and ataxia) were observed in one male at the highest dose tested, a finding that was consistent with the multi-organ toxicity observed at this dose. No morphological changes in the testes were observed in dogs at any dose. The NOAEL was considered to be 200 ppm, equivalent to 6 mg/kg bw/d in males and 5 mg/kg bw/d in females.

In rats, the testes were the target organ following subchronic oral treatment (14 weeks) at a high dose. Abnormal spermatozoa and hypospermia in the epididymis, decreased testicular weight, and testicular degeneration and vacuolation in males were observed after 90 days of exposure at 10000 ppm (616 mg/kg bw/d). These effects proved to be reversible in most animals after cessation of treatment. Other effects in subchronically treated rats were limited to declines in terminal body weight in 10000 ppm male rats and an increased incidence of accumulation of alveolar macrophages in both sexes at 10000 ppm. Thyroid and thymus were unaffected in rats at any dose. The NOAEL was considered to be 2500 ppm, equivalent to 148 mg/kg bw/d in male and 188 mg/kg bw/d in female rats.

Unlike the rat, no adverse effects of any kind were observed in mice tested orally up to the limit dose. In vitro results from a comparative metabolism study using hepatocytes from male rats, mice, and humans revealed species differences in the metabolism of spirotetramat. Specifically, mouse hepatocytes were better able than rat or human liver cells to metabolize BYI 08330-enol via glucuronidation. Potentially lower levels of the enol metabolite in mice in vivo may account for the lack of testicular toxicity observed in this species. The NOAEL was considered to be 7000 ppm, equivalent to 1305 mg/kg bw/d in males and 1515 mg/kg bw/d in females.

Subchronic exposure of rats by the dermal route yielded no evidence of systemic toxicity when spirotetramat was tested up to 1000 mg/kg bw/day.

Long-Term toxicity and carcinogenicity

Chronic toxicity/carcinogenicity was tested in rats and mice following application of spirotetramat for one and two years, respectively. Target organs in rats were the kidney (both sexes) at mid and high doses and the liver (females) at the highest dose only. These results are consistent with the excretory and/or detoxification roles of the kidney and liver. Consistent with the subchronic study the lung demonstrated treatment-related presence of alveolar macrophages in mid and high dose males and high dose females. Testicular histopathology in rats was not observed following 12 months of oral exposure; however, after 24 months of treatment with spirotetramat, spermatid degeneration in the testes and germ cell exfoliated debris in the epididymis were observed in male rats at the high dose only (7500 ppm; 373 mg/kg bw/day).

In the last month of the one year chronic toxicity study, 10 rats/sex/dose were evaluated in an FOB assessment that included evaluation of motor activity and responses to sensory stimuli. Treatment-related effects in the FOB assessments were not observed.

No adverse findings were observed in mice up to the limit dose following long-term treatment with spirotetramat.

Treatment-related increases in tumor incidence were not observed in either sex in rats or mice.

Reproductive and Developmental Toxicity

In addition to testicular histopathology observed following subchronic and chronic exposure of male rats to spirotetramat, evidence of male reproductive toxicity was provided in the 2-generation reproductive toxicity study. Abnormal sperm cells were reported in F1-generation male rats treated with 6000 ppm (419 mg/kg bw/day) spirotetramat in the diet, and decreased reproductive performance was also observed in one of these males. Similar results were obtained in the 1-generation reproductive toxicity range-finding study, in which decreased sperm motility and progression and increased abnormal sperm cells in the epididymides were observed in F1 males at ≥6000 ppm (320 mg/kg bw/day). The highest dose level of 10000 ppm, equivalent to 538 mg/kg bw/d, was associated with no fertility in parental generation animals. There were no implantation sites noted in the females due to treatment-related effects on sperm cells of males at this dose level (increased numbers of abnormal sperms, reduced epididymal sperm counts, decline in both motility and progression of epididymal sperm cells). Absolute and relative weight of the cauda epididymis was decreased in parental males. Histopathology showed abnormal sperm cells of minimal to moderate severity in the epididymis and the cauda epididymis.

Renal toxicity was also observed in F1 adults in the 2-, but not 1-generation reproductive toxicity study. Offspring toxicity was limited to decreased body weights in both studies, observed in F_1 and F_2 pups respectively of both sexes during lactation at 6000 ppm (320 and 419.3 mg/kg bw/day respectively). Decreased body weights were also observed in parental animals at the same dose. The difference in dose between the two studies was attributed to increased food consumption of parental animals in the 2-generation study.

Development of the sexual organs of offspring (balano-preputial separation, vaginal opening) was unaffected in both studies. Developmental toxicity in the absence of maternal toxicity was not observed in either the rat or rabbit.

In February 2008 the notifier submitted a position paper (*High dose reproductive effects in male rats and their relevance to humans; Temerowski M., 2008*). It was stated that the effects on testicular spermatogenesis were attributed to the BYI 08330-enol, which is the main metabolite in the rat. BYI 08330-enol is further metabolised by oxidation reactions to BYI 08330-desmethylenol, BYI 08330-enol-alcohol and BYI 08330-ketohydroxy. Oxidation products accounted for approximately 14%. Conjugation was not detected. In the mouse, conjugation of BYI 08330-enol with glucuronic acid accounted for approximately 30%. In human liver cells, conjugation to BYI 08330-enol-glucuronic acid was 6%. The in vitro conjugation rate is dependent on the concentration used and declined in mice from 30% to 9% and in humans from 6% to 2% at liver concentrations of 19 µg/g and 190 µg/g BYI 08330, respectively. Glucuronidation of the BYI 08330-enol in mice leads to much lower systemic levels of free BYI 08330-enol when compared to the rat. The conjugation enables the mouse to utilize separate active transport systems in the kidneys, thus avoiding a saturation of the elimination process. Thus, the utilization of different transport systems renders the mouse less sensitive to BYI 08330-mediated testicular toxicity when compared to the rat. Based on the metabolic similarity between mice and humans, it is likely that humans are also less sensitive to BYI 08330-mediated testicular toxicity than rats.

This statement of the notifier can not be agreed to. In contrast to mice, for humans the ability to conjugate BYI 08330-enol with glucuronic acid is fivefold lower than for the mouse (dependent on the concentration, in humans 6% respectively 2%, in mice 30% respectively 9%). Therefore a similarity in the metabolic pathway can not be followed. As for humans conjugation is only 2% at high doses, it can not be assumed that humans are less sensitive to Spirotetramat than rats.

Due to abnormal sperm cells, decreased sperm motility and progression and decreased reproductive performance, spirotetramat should be classified to "category 3 of reproductive

substances“ and labelled with the risk phrase “R 62 – Possible risk of impaired fertility“ according to Annex VI of the EC Council Directive 67/548/EEC.

In the developmental toxicity study in rats, toxicity to the offspring was observed in the presence of maternal toxicity, including decreased food consumption and body weight/gain, at 1000 mg/kg bw/day. Reduced fetal weight and increased incidences of skeletal malformations and skeletal deviations were observed at 1000 mg/kg bw/day. Malformations at the high dose included one case of supernumerary lumbar vertebra, one case of cleft palate and one case of co-arctation of aortic arch. One case of atrial septal defect of the heart and microphthalmia were observed in the control, low and high dose each, but not at the mid dose.

Four cases of dysplastic forelimb bones (1.5 %) and three cases of malformed sacral vertebral arches with pelvic shift (1.1 %) were observed in the high dose. Historical control data of the performing laboratory (Bayer HealthCare AG) for dysplastic forelimb bones in studies conducted in the years 1999 – 2004 showed 26 affected animals out of 1975 animals, a percentage of 1.3 % [range 0.4 – 4.3% due to one study conducted in the year 2000, were 10 animals out of 232 were affected (4.3%)]. An incidence of 1.5 % in the study with spirotetramat is therefore outside the concurrent control (0.4%) and the historical control data (1.3%).

Statistically significantly increased incidences of sacral vertebral alterations (1.1 %) were observed at a dose level of 1000 mg/kg bw spirotetramat in comparison to the concurrent controls (0.0 %). The incidence in historical controls in studies conducted 1999 – 2006 showed 2 affected animals out of 6554 animals, a percentage of 0.03 % (range 0 – 0.4%).

Statistically significantly increased incidences of wavy ribs were observed at all dose levels compared to concurrent and historical control values. Statistically significantly increased numbers of fetuses with 14th ribs were observed at a dose level of 1000 mg/kg/d spirotetramat.

The maternal and the developmental NOAEL for this study was set at 140 mg/kg bw/d. Due to increased incidences of skeletal malformations and skeletal deviations and according to Annex VI of the EC Council Directive 67/548/EEC, spirotetramat should be classified to “category 3 of reproductive substances“ and labelled with the risk phrase “R 63 – Possible risk of harm to the unborn child“.

In the developmental toxicity study in rabbits, offspring toxicity was not observed at any dose up to 160 mg/kg bw/day. However, maternal toxicity was observed at ≥40 mg/kg bw/day, including a dose-dependent increase in abortion and clinical signs of toxicity in affected animals (severely reduced food consumption, body weight loss, alopecia, altered appearance of feces, discoloured urination). Gross pathology revealed treatment-related fluid/gaseous contents in caecum, mottled gall bladder, discolouration of the liver. The maternal NOAEL was set at 10 mg/kg bw/d.

Genotoxicty

Overall, assays for point mutations and chromosomal aberrations (both *in vivo* and *in vitro*) were negative for spirotetramat. A weak positive finding was noted in a single in vitro chromosomal aberration test, but at cytotoxic concentrations only. Negative findings in two in vivo chromosomal aberration studies and one in vivo/in vitro unscheduled DNA synthesis assay using rat hepatocytes do not suggest a genotoxic concern for spirotetramat.

Neurotoxicity

Spirotetramat has been assessed for potential neurotoxicity in two acute neurotoxicity studies in the rat and was shown to have no neurotoxic potential in these studies. In the first acute neurotoxicity study, rats received single oral doses of 0, 200, 500 or 2000 mg/kg bw spirotetramat via gavage. Evidence of acute oral toxicity was observed in both sexes at all

dose levels but was limited to clinical signs (urine and perianal stain) and decreased activity in the figure-eight maze beginning on the day of treatment and with complete recovery by day 7.

In a follow-up study, rats received single oral doses of 0, 50, 100 or 500 mg/kg bw spirotetramat via gavage. The findings from the first study were confirmed at a dose level of 500 mg/kg bw. No compound-related effects were observed at 50 and 100 mg/kg bw.

The NOAEL for systemic effects in this study was established at 100 mg/kg bw spirotetramat. Neurotoxic effects were not observed up to a limit dose of 2000 mg/kg bw.

Mechanistic studies

In a mechanistic study designed to explore the time of onset of testicular toxicity of spirotetramat in rats, decreased epididymal sperm counts were recorded ≥10 days of treatment with 1000 mg/kg bw/day by gavage. Repeated dosing, therefore, is necessary to produce male reproductive toxicity in rats.

In a second mechanistic study, male rats were treated by gavage with the enol metabolite of spirotetramat for 21 days at a dose of 800 mg/kg bw/day. Spermatotoxicity, abnormal sperm, and Sertoli cell vacuolation were observed in the testes-epididymides of treated animals. Therefore, male reproductive toxicity in rats is likely due to the enol metabolite of spirotetramat.

PUBLIC HEALTH STANDARDS

Poison Scheduling

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

On the basis of its low acute toxicity, severe eye irritation and skin sensitisation potential, the NDPSC has included spirotetramat in schedule 6 of the Standard for the Uniform Scheduling of Drugs and Poisons (SUSDP). There are provisions for appropriate first-aid instructions and safety directions on the product label.

No-Observed-Effect-Level (NOEL) and Acceptable Daily Intake (ADI)

The ADI is that quantity of an agricultural compound which can safely be consumed on a daily basis for a lifetime and is based on the lowest NOEL obtained in the most sensitive species. This NOEL is then divided by a safety factor which reflects the quality of the toxicological database and takes into account the variability in responses between species and individuals.

The ADI for spirotetramat was established at 0.05 mg/kg bw/day based on a NOEL of 5 mg/kg bw/day in a one-year oral dog study and using a 100-fold safety factor in recognition of the extensive toxicological database available for spirotetramat.

Acute Reference Dose (ARfD)

The acute reference dose is the maximum quantity of an agricultural or veterinary chemical that can safely be consumed as a single, isolated, event.

An Acute Reference Dose (ARfD) of 1 mg/kg bw/d was set for spirotetramat by applying a 100-fold safety factor to a NOEL of 100 mg/kg bw/d established in an acute neurotoxicity study in rats.

RESIDUES ASSESSMENT

Introduction

Movento 240 SC Insecticide contains the new active constituent spirotetramat (Figure 1) and is proposed for use to control silverleaf whitefly in Brassica crops. As part of the residues assessment for spirotetramat, plant and animal metabolism studies, supervised residue trials, trade aspects, environmental fate and chemistry were considered.

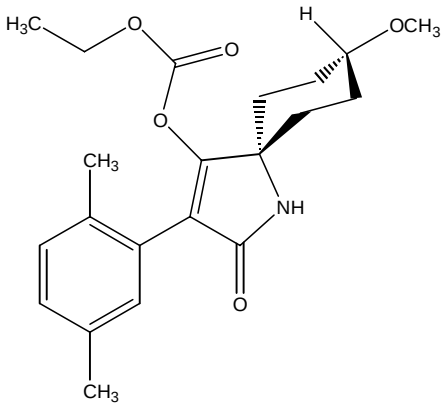


Figure 1: Spirotetramat

METABOLISM

Plants

The metabolism of spirotetramat was investigated in 4 different crops (apple, cotton, lettuce and potatoes), using spirotetramat labelled with ^{14}C at the 3 position of the pyrroline moiety.

Apple

The metabolism of spirotetramat was investigated in apple (fruits & leaves) following two spray applications of [azaspirodecenyl-3-^{14}C]spirotetramat, formulated as an oil-dispersion formula (100 OD), at a total target rate of 1152 g a.i./ha (actual applied 1100 g a.i./ha). The first application was at a growth stage 69 of the current BBCH code and the second application was 20 days later at growth stage 71, 63 days before harvest.

At harvest the total radioactive residue (TRR) amounted to 0.61 mg/kg in apple and 36.63 mg/kg in apple leaves. Approximately 49% of the TRR in apple was surface residue, and washed off with dichloromethane. Washed apple was extracted with acetonitrile (ACN)/water, and 49.5% of the TRR was in the extract, leaving only 2.1% of the TRR (0.01 mg/kg) as unextracted residues. Unchanged parent spirotetramat (48.5% of the TRR, 0.3 mg/kg) was the only residue detected in the surface wash. The predominant residue found in the extract was BYI 08330-mono-hydroxy (15.6% of TRR, 0.1 mg/kg) followed by BYI 08330-ketohydroxy (7.7% of TRR, 0.05 mg/kg), BYI 08330-di-hydroxy (4.4% of TRR, 0.03 mg/kg), BYI 08330-desmethyl-ketohydroxy (3.8% of TRR, 0.02 mg/kg), BYI 08330-enol (2.1% of TRR, 0.01 mg/kg), and the respective glycosides thereof (5.1% of TRR, 0.03 mg/kg).

As in apple fruits, the major residue in apple leaves was the unchanged spirotetramat (72% of the TRR). Other residues detected were BYI 08330-ketohydroxy, BYI 08330-enol, and glycoside isomers of BYI 08330-desmethyl-ketohydroxy. A BYI 08330-ketohydroxy-formiate-glycoside was also detected.

Cotton

The metabolism of spirotetramat was investigated in cotton (gin trash, lint & undelinted seeds) following two spray applications of [azaspirodecenyl-3-^{14}C]spirotetramat, formulated as a suspension concentrate (240 SC), at a target total rate of 312 g a.i./ha (0.28 lbs. a.i./A, actual applied 264 g a.i./ha/season (0.23 lbs. a.i./A)). The first application was made at an early growth stage (BBCH 15) at a rate of 96 g a.i./ha, and the second at growth stage 85 (about 50% of bolls open, 134 days interval) at a rate of 216 g a.i./ha. One immature cotton plant sample was collected at 19 days after the first application. Cotton gin trash, lint and undelinted seed samples were harvested 39 days after the last treatment.

The total radioactive residue (TRR) was 2.381 mg/kg in the immature plant sample, 1.641 mg/kg in gin trash, 1.078 mg/kg in lint, and 0.119 mg/kg in undelinted seed. Parent compound, spirotetramat, was the major residue (46.95% of the TRR, 1.117 mg/kg) identified in the immature cotton plant. Also identified were 13 minor metabolites ranging from 0.18% to 9.76% of the TRR (0.004-0.232 mg/kg).

In cotton gin trash, the major residues identified were BYI 08330-ketohydroxy (29.7% of the TRR; 0.478 mg/kg), spirotetramat (19.8% of the TRR; 0.319 mg/kg), and BYI 08330-enol (12.1% of the TRR; 0.196 mg/kg). In cotton lint, the major residues identified were spirotetramat (32.3% of the TRR; 0.348 mg/kg), BYI 08330-mandelic acid amide (11.9% of the TRR; 0.128 mg/kg), and BYI 08330-ketohydroxy (10.5% of the TRR; 0.113 mg/kg). The major residue found in the cotton undelinted seeds was BYI 08330-enol (39.8% of the TRR; 0.047 mg/kg), while BYI 08330-ketohydroxy represented 9.04% of the TRR (0.011 mg/kg). Ten metabolites representing 0.6-4.4% of the TRR (0.003-0.064 mg/kg) were also identified in the gin trash, lint and undelinted seeds.

Lettuce

The metabolism of spirotetramat was investigated in head lettuce following two spray applications of [azaspirodecenyl-3-^{14}C]spirotetramat, formulated as an oil-dispersion formula (100 OD), at a target total rate of 144 g a.i./ha (0.13 lbs. a.i./A, actual total rate applied was 167 g a.i./ha (0.15 lbs a.i./A)). The two applications were made at a 14-day retreatment interval. Treated lettuce was harvested at maturity 7 days after the last treatment.

Greater than 95% of the total radioactive residue (TRR) in lettuce was extracted with acetonitrile (ACN)/water. The TRR was 3.13 mg/kg, calculated by summing extracts and post extraction solids. Over 91% of the extracted radioactivity was identified. Unchanged parent compound spirotetramat was the major residue identified (55.9% of the TRR; 1.75 mg/kg), followed by BYI 08330-enol (17.8% of the TRR; 0.56 mg/kg), BYI 08330-enol-glucoside (11.4% of the TRR; 0.36 mg/kg), and BYI 08330-ketohydroxy (6.2% of the TRR; 0.2 mg/kg).

Potatoes

The metabolism of spirotetramat was investigated in potatoes (tuber & tops) following three spray applications of [azaspirodecenyl-3-^{14}C]spirotetramat, formulated as an oil dispersion (100 OD), at a target total rate of 288 g a.i./ha (0.26 lbs. a.i./A, actual applied amount was 308 g a.i./ha (0.27 lbs. a.i./A)). The applications were made at a 21-day re-treatment interval (RTI). Potato samples were harvested 14 days after the last treatment.

Approximately 80% of the total radioactive residue (TRR) in tuber, and 96% of the TRR in tops were extracted with acetonitrile(ACN)/water. Enzymatic treatment of the extracted tuber further released approximately 14% of the TRR. The TRR in tuber and tops was 0.255 mg/kg and 11.057 mg/kg, respectively, calculated by summing extracts and post extraction solids.

Parent spirotetramat was not identified in potato tuber, the predominant metabolite identified was BYI 08330-enol (65.8% of the TRR, 0.168 mg/kg), followed by BYI 08330-ketohydroxy (6.8% of the TRR, 0.018 mg/kg) and BYI 08330-desmethyl-enol (6.7% of the TRR, 0.018 mg/kg) and several other minor metabolites (≤2.5 % of the TRR, 0.006 mg/kg).

In potato tops, spirotetramat and BYI 08330-ketohydroxy were the major residues identified, represented 49.4% and 24.8% of the TRR, respectively. BYI 08330-enol (7.8% of the TRR) and several other minor metabolites (≤3.6% of the TRR) were also identified.

Plant metabolism summary

The major reaction involved in degradation of the parent compound was hydrolysis of the side chain ester bond resulting in the formation of BYI 08330-enol (Figure 2). The enol is then further hydroxylated in the pyrroline moiety leading to the formation of BYI 08330-ketohydroxy, or is subsequently conjugated with glucose to yield BYI 08330-enol glucoside. Demethylation of BYI 08330-enol results in formation of BYI 08330-4-desmethyl-enol which is further oxidised to the BYI 08330-desmethyl-keto-hydroxy metabolite. These metabolites may be further conjugated with a hexose. An important reaction in apples was conversion of BYI 08330-enol to BYI 08330-mono-hydroxy. For cotton cleavage of the pyrroline ring of BYI 08330-ketohydroxy followed by decarboxylation and hydrolysis yielded BYI 08330-MA-amide, BYI 08330-olefin, BYI 08330-mandelic acid amide, and BYI 08330-mandelic acid.

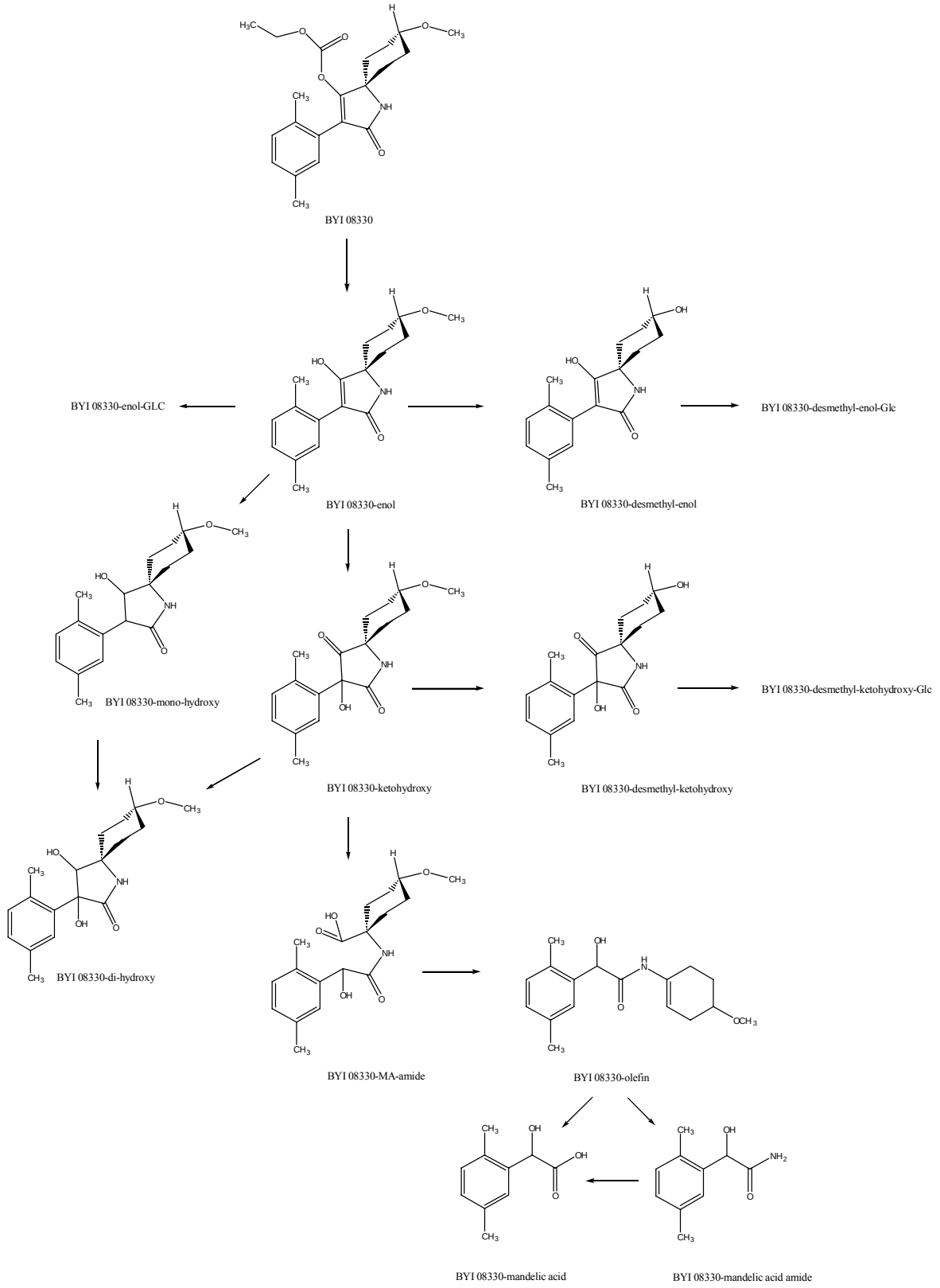


Figure 2: Summary of metabolism of spirotetramat in plants.

Confined Rotational Crops

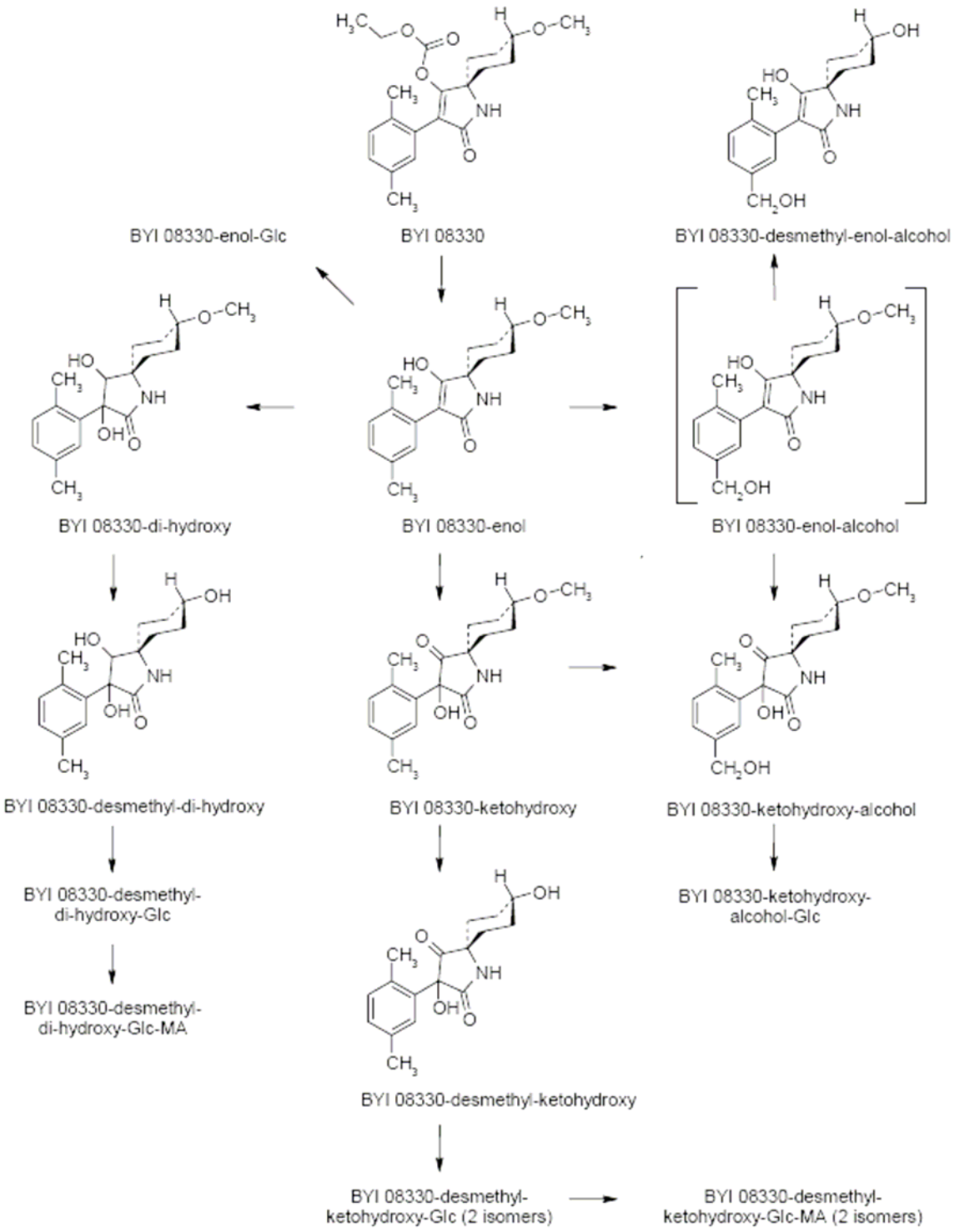
The metabolism in rotational crops (spring wheat, Swiss chard and turnips) was investigated following spray application of [azaspirodecenyl-3-^{14}C] spirotetramat onto bare soil (day 0) at an application rate of 406 g a.i./ha (0.36 lbs. a.i./A). Crops were sown at day 30, day 135, and day 260. The total radioactive residues (TRRs) are summarised in Table 1. TRRs were highest in wheat straw of the 30-day rotation (0.998 mg/kg) followed by wheat hay (0.384 mg/kg), turnip leaves (0.123 mg/kg), Swiss chard (0.078 mg/kg), wheat grain (0.026 mg/kg), wheat forage (0.024 mg/kg), and turnip roots (0.021 mg/kg). A significant decline of TRRs from the 30-day to the 260-day rotation was observed in all raw agricultural commodities (RACs). In the 260-day rotation, only wheat hay and wheat straw showed residues above 0.01 mg/kg.

Table 1: Total radioactive residues in rotational crops (in mg/kg)

Plant-back interval (days)	Wheat				Swiss chard	Turnip	
	forage	hay	straw	grain		tops	roots
30	0.024	0.384	0.998	0.026	0.078	0.123	0.021
135	0.021	0.038	0.097	0.010	0.012	0.015	0.003
260	0.009	0.014	0.036	0.002	0.006	0.008	0.002

Parent compound spirotetramat was not detected in any sample. Major metabolites (>10% of the TRR) in the 30-day and 135-day rotation were: BYI 08330-ketohydroxy, BYI 08330-desmethyl-ketohydroxy-Glc (two isomers), BYI 08330-desmethyl-ketohydroxy-Glc-MA (two isomers), BYI 08330-desmethyl-dihydroxy-Glc, BYI 08330-desmethyl-di-hydroxy-Glc-MA, and BYI 08330-di-hydroxy. Other identified metabolites were of minor importance (<10% of TRR).

The proposed metabolic pathway for spirotetramat in rotational crops is shown in figure 3. It appears that two major metabolic routes in rotational crops start with the soil metabolites BYI 08330-ketohydroxy and BYI 08330-enol. The first metabolic route proceeds by demethylation of the cyclohexyl ring or hydroxylation of one methyl group of the xylol ring. Another metabolic route starts with the addition of water to the tetramic acid ring of BYI 08330-enol resulting in the formation of BYI 08330-di-hydroxy, followed by the demethylation of the metabolite. Additionally, hydroxylation of one methyl group of the xylol ring of BYI 08330-enol followed by demethylation of the cyclohexyl ring results in BYI 08330-desmethyl-enol-alcohol, which was detected in all matrices. Most of the metabolites were rapidly conjugated.



[ ] structure in brackets was postulated as intermediate.

Figure 3: Proposed metabolic pathway for spirotetramat in rotational crops.

Animals

Studies were conducted on the metabolism of spirotetramat in lactating goats and laying hens. Details are provided below.

Laying Hens

Six laying hens were dosed orally once daily by gavage with [azaspirodecenyl-3-^{14}C]spirotetramat at a rate of 1.01 mg a.i./kg bw/day (corresponded to 12.86 ppm in feed) for 14 days.

The majority of the radioactivity (90% of the administered dose (AD)) was detected in the excreta. Only 0.045% and 0.023% of the total AD were detected in the eggs and edible organs/tissues, respectively. The TRR in eggs reached a plateau by 4 – 8 days after the first administration. The highest total radioactive residue (TRR) was detected in kidneys (0.039 mg/kg) and liver (0.017 mg/kg), followed by fat (0.004 mg/kg), and muscle (0.003 mg/kg). The average TRR in eggs was 0.015 mg/kg.

Aliquot samples from the egg pool, combined muscle, subcutaneous fat and liver were used for metabolite analysis. The parent compound was not detected in any of the samples. BYI 08330-enol was the major metabolite detected in eggs, liver, fat and muscle (18-84% of the TRR). The glucuronic acid conjugate BYI 08330-enol-GA was also detected in eggs (6.9% of the TRR, 0.001 mg/kg), muscle (4.2% of the TRR, <0.001 mg/kg) and liver (15.1% of the TRR, 0.003 mg/kg). One non-polar metabolite was the main component in extracts of fat (56.5% of TRR, 0.002 mg/kg). The metabolite underwent alkaline hydrolysis forming 2 components. The applicant suggested that the metabolite is a fatty acid conjugate.

Lactating goats

The nature of the residue in milk and foodstuffs originating from ruminants was investigated with a lactating goat following 4 daily oral administrations of [azaspirodecenyl-3-^{14}C]spirotetramat at a mean dose rate of 2.22 mg a.i./kg bw/day (73.03 ppm in feed) given by gavage.

Approximately 90% of the administered dose (AD) was eliminated via urine (78.4%) and faeces (11.6%). The highest total radioactive residue (TRR) was observed in kidney (0.1835 mg/kg) and liver (0.0496 mg/kg). Significantly lower residues were detected in the muscle: round muscle (0.0113 mg/kg), flank muscle (0.0085 mg/kg), and loin muscle (0.0083 mg/kg); and fat: subcutaneous fat (0.0078 mg/kg), omental fat (0.0030 mg/kg), and perirenal fat (0.0026 mg/kg). While the TRR in subcutaneous fat was at similar levels to those in muscle, the TRRs of omental and perirenal fat were significantly lower. The TRR in milk samples was in the range of 0.0038-0.0261 mg/kg, reaching a plateau level within the observation period of 96 hours.

Aliquots of milk, combined muscle, combined fat; liver and kidney were taken for metabolite analysis. The parent compound was not detected in any of the milk and the edible tissue/organ samples. The major metabolites detected were BYI 08330-enol (33.7-78.4% of the TRR) and BYI 08330-enol-glucuronide (≤37% of the TRR). Three other minor metabolites (BYI 08330-ketohydroxy, BYI 08330-desmethyl-enol, and BYI 08330-mono-hydroxy) were found at low levels (<10% of the TRR).

Animal metabolism summary

The pathways for degradation of spirotetramat was similar in hens and goats and involved cleavage of the ester group to give BYI 08330-enol, followed by conjugation of the enol hydroxy group with glucuronic acid to form BYI 08330-enol-GA (Figure 4). Oxidation of the

azaspirodecenyl moiety to BYI 08330-ketohydroxy and demethylation of the methoxy group to BYI 08330-desmethyl-enol were minor metabolic reactions as well as reduction of the azaspirodecenyl moiety to BYI 08330-monohydroxy (goat only).

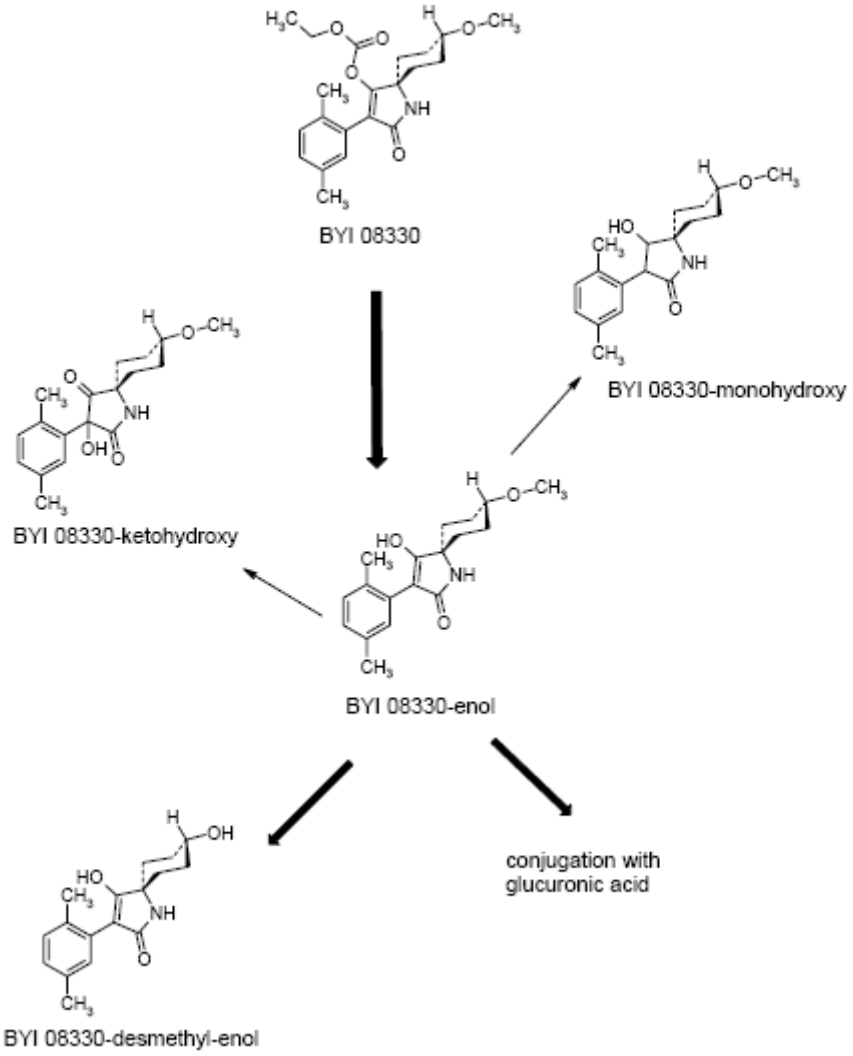


Figure 4: Proposed metabolic pathway for spirotetramat in target animals
(BYI 08330-monohydroxy detected in goat only)

ANALYTICAL METHODS

Commodities of plant origin

In Australian trials on Brassicas residues of BYI-08330 (spirotetramat), BYI-08330-enol, BYI-08330-keto-hydroxy, BYI-08330-mono-hydroxy and BYI-08330-enol-glucoside were extracted from homogenised samples with acetonitrile containing 0.02% v/v formic acid. The extract was filtered using a polyethylene frit and diluted with acetonitrile / formic acid solution. Quantitation of residues was by liquid chromatography coupled to a triple quadrupole mass spectrometer scanning in MS/MS mode with internal standards. The LOQ for the method was 0.02 mg/kg for spirotetramat and each of its metabolites. The LOQ was 0.11 mg/kg when expressed as total spirotetramat equivalents.

Commodities of animal origin

The parent compound spirotetramat and the metabolites BYI 08330-enol, and BYI 08330-enol-GA residues were extracted from milk samples (whole, milk fat, and skim milk) by blending with Celite® and acetonitrile containing 0.22 mL/L formic acid. Stable labelled internal standard was added to the blended extract which was then purified by C18 solid-phase extraction. An aliquot of the eluate was concentrated and reconstituted in water containing 0.22 mL/L formic acid for analysis by LC-MS/MS.

The total spirotetramat residues were extracted from tissue samples by blending with acetonitrile:water (7:3 v/v) containing 0.22 mL/L formic acid. An aliquot of stable labelled internal standard was added to the blended extract along with some Celite®. After stirring, the solids were allowed to separate to the bottom. An aliquot of the supernatant was concentrated and reconstituted in water containing 0.22 mL/L formic acid for analysis by LC-MS/MS. The LOQ for spirotetramat and the metabolites BYI 08330-enol and BYI 08330-enol-GA was 0.005 mg/kg for milk matrices and 0.010 mg/kg for tissue matrices.

Stability of pesticide residues in stored analytical samples

The applicant has provided storage stability studies for tomato (fruit and paste), potato (tuber), lettuce (head), climbing French bean (bean with pod) and almond (nutmeat). Samples were spiked separately with spirotetramat, BYI 08330-enol and BYI 08330-ketohydroxy at spiking levels of 0.2 mg/kg (each analyte) and with a mixture of BYI 08330-mono-hydroxy and BYI 08330-enol-glucoside (0.2 mg/kg each). Samples were stored at -18ºC for up to 540 days.

Residues of BYI 08330-ketohydroxy, -mono-hydroxy and -enol-Glc were stable (<30% degradation) in all matrices analysed for the duration of the storage stability study. Residues of the parent, spirotetramat, were stable in tomato fruit and paste, but declined by 80% in potato tubers and almond nutmeats, 60% in head lettuce, and 70% in climbing French bean. Residues of BYI 08330-enol were stable in tomato fruit and paste and almond nutmeat, but declined by 40% in potato tubers, head lettuce, and climbing French bean. However, total residues (calculated as the summation of the single spiked analyte and all detectable analytes resulting from the degradation of the spiked compound) were stable (<30% degradation) in tomato fruit, potato tubers, lettuce heads, climbing French bean, and almond nutmeat during frozen storage for up to 540 days.

RESIDUE DEFINITION

Commodities of plant origin

In the plant metabolism studies unchanged parent was the major residue in apple fruit (51.3% of TRR, 0.32 mg/kg) and leaves (72% of TRR, 26.4 mg/kg), cotton lint (32.3% of TRR, 0.348 mg/kg), lettuce (55.9% of TRR, 1.75 mg/kg) and potato leaves (49.4% of TRR, 5.45 mg/kg). BYI-08330-enol was the major residue in cotton seed (39.8% of TRR, 0.047 mg/kg) and

potato tubers (54.9% of TRR, 0.14 mg/kg). Other metabolites that were found in significant amounts (>10% of TRR) in plant matrices were BYI 08330-enol-glucoside (11.4% of TRR in lettuce, 0.36 mg/kg), BYI 08330-ketohydroxy (29.6 % of TRR in cotton gin trash, 0.478 mg/kg; 24.8% of TRR in potato leaves, 2.74 mg/kg) and BYI 08330-monohydroxy (15.6% of TRR in apple fruit, 0.1 mg/kg). BYI 08330 mandelic acid amide was also found at 11.87% of the TRR (0.128 mg/kg) in cotton lint. However, cotton lint is not used for human consumption or as an animal feedstuff. As mandelic acid amide was not detected in any other plant matrices it will not be included in the residue definition at this time. In the health risk assessment, the Office of Chemical Safety identified the following compounds as toxicologically relevant for the residue definition: spirotetramat, BYI 08330-enol, BYI 08330-ketohydroxy, BYI 08330-monohydroxy and BYI 08330-enol glucoside.

Adequate analytical methodology has been provided for the determination of spirotetramat, BYI 08330-enol, BYI 08330-ketohydroxy, BYI 08330-monohydroxy and BYI 08330-enol glucoside in commodities of plant origin. However, it is recognised that a complex residue definition may cause problems for analysts monitoring samples for compliance purposes. Separate residue definitions will therefore be recommended for plant commodities for dietary exposure assessment and enforcement purposes.

The following residue definition is recommended for spirotetramat for commodities of plant origin for dietary exposure assessment purposes:

Sum of spirotetramat, BYI 08330-enol, BYI 08330-ketohydroxy, BYI 08330-monohydroxy and BYI 08330-enol-Glc, expressed as spirotetramat.

For enforcement purposes the mono-hydroxy and enol-Glc metabolites may be excluded from the residue definition as the mono-hydroxy was <LOQ in all the Brassica trials provided with the application. The enol-Glc metabolite was generally close to or below the LOQ in the Brassica residue trials with a few exceptions. The ketohydroxy metabolite was found at significant levels in a few of the residue trials, especially for Brussels sprouts. The enol metabolite was present at significant levels in the remaining Brassica residue trials.

In addition, residue data for other vegetable crops, citrus, mangoes and cotton have also been supplied previously to the APVMA. This data indicates that it is the enol metabolite which makes the major contribution to the total residue, often when the ketohydroxy metabolite is present at much lower levels. It is therefore considered that the enol metabolite, together with the parent are sufficient as marker residues for compliance purposes. The following residue definition is recommended for spirotetramat for commodities of plant origin for enforcement:

Sum of spirotetramat and BYI 08330-enol, expressed as spirotetramat.

Rotational crops

In the confined rotational crop study major metabolites (>10% of the TRR) in the 30-day and 135-day rotation were: BYI 08330-ketohydroxy, BYI 08330-desmethyl-ketohydroxy-Glc (two isomers), BYI 08330-desmethyl-ketohydroxy-Glc-MA (two isomers), BYI 08330-desmethyl-dihydroxy-Glc, BYI 08330-desmethyl-di-hydroxy-Glc-MA, and BYI 08330-di-hydroxy. Other identified metabolites were of minor importance (<10% of the TRR). Not all of the significant metabolites have been included in the residue definition for commodities of plant origin. However in the field rotation study, no residues were detected in rotaional crops planted at a 30 day plant back interval after the last application of spirotetramat to the primary crop. Metabolites present in rotational crops are indicative of a greater degree of metabolism. The metabolism and residue studies indicate that residues in rotational crops are not expected and thus the proposed residue definitions for commodities of plant origin remain appropriate.

Commodities of animal origin

In the hen and goat metabolism studies only 3 metabolites were detected at > 10% of the TRR in organs, tissues, milk and eggs. The major metabolite was BYI 08330-enol which was detected at up to 78% of the TRR in goat kidney and 84% of the TRR in hen eggs. The glucuronic acid conjugate BYI 08330-enol-GA was also significant accounting for 15.1% of the TRR in hen liver and 37.4% of the TRR in goat liver. An unknown metabolite was also detected at 56.5% of the TRR in combined hen fat. However, as this metabolite was only present at 0.002 mg equiv./kg it will not be considered for the residue definition for commodities of animal origin.

Adequate analytical methodology has been provided for the determination of spirotetramat, BYI 08330-enol and it glucuronic conjugate BYI 08330-enol-GA in commodities of animal origin. The following residue definition is recommended for spirotetramat for commodities of animal origin for dietary exposure assessment purposes:

Sum of spirotetramat, BYI 08330-enol and BYI 08330-enol-GA, expressed as spirotetramat.

In the animal transfer study provided with the application the enol metabolite was the dominant residue. The enol-GA was detected at lower levels and was only present at the same time as the enol. It is considered that the enol is a suitable marker for the enol-GA metabolite and that the following residue definition can be recommended for commodities of animal origin for enforcement:

Sum of spirotetramat and BYI 08330-enol, expressed as spirotetramat.

The following entry to Table 3 of the MRL Standard is appropriate for spirotetramat:

Table 3

Compound	Residue
ADD: Spirotetramat	For enforcement: Sum of spirotetramat, and cis-3-(2,5-dimethylphenyl)-4-hydroxy-8-methoxy-1-azaspiro[4.5]dec-3-en-2-one, expressed as spirotetramat. Commodities of plant origin for dietary exposure assessment: Sum of spirotetramat, cis-3-(2,5-dimethylphenyl)-4-hydroxy-8-methoxy-1-azaspiro[4.5]dec-3-en-2-one, cis-3-(2,5-dimethylphenyl)-3-hydroxy-8-methoxy-1-azaspiro[4.5]decane-2,4-dione, cis-3-(2,5-dimethylphenyl)-4-hydroxy-8-methoxy-1-azaspiro[4.5]decan-2-one and the glucoside of cis-3-(2,5-dimethylphenyl)-4-hydroxy-8-methoxy-1-azaspiro[4.5]dec-3-en-2-one, expressed as spirotetramat. Commodities of animal origin for dietary exposure assessment: Sum of spirotetramat, cis-3-(2,5-dimethylphenyl)-4-hydroxy-8-methoxy-1-azaspiro[4.5]dec-3-en-2-one and the glucuronic acid conjugate of cis-3-(2,5-dimethylphenyl)-4-hydroxy-8-methoxy-1-azaspiro[4.5]dec-3-en-2-one, expressed as spirotetramat.

RESIDUES TRIALS

Twelve Australian trials were conducted on Brassica vegetables in 2005/06. Two trials were conducted on Brussels sprouts, 6 on cabbage and 4 on broccoli. Details are given below.

Brussels sprouts

Two residues trials were conducted on Brussels sprouts grown at Coldstream, Victoria and Nairne in South Australia in 2005. Three applications of a 240 SC formulation of spirotetramat were made at 48, 96 or 144 g ai/ha, or at 4.8, 9.6 or 14.4 g ai/100 L at weekly intervals, just prior to crop maturity. Spray volumes ranged from 740 – 904 L/ha for the broadcast applications. For the dilute applications to the point of run off, spray volumes ranged from 1880 – 2840 L/ha. Samples of Brussels sprouts buttons were collected nominally at 7 days after the second application and at 0, 1, 3 and 7 days after the third application at crop maturity.

Total spirotetramat residues in Brussels sprouts immediately before the 3rd application at 96 g ai/ha (1× proposed rate) were 0.15 and 0.21 mg/kg. Immediately after the 3rd application at this rate total residues were 0.32 and 0.52 mg/kg, suggesting that a significant proportion of the residue was due to the earlier applications. At the proposed 3 day withholding period after the last of 3 applications at 96 g ai/ha (1× proposed rate) total residues were 0.48 and 0.83 mg/kg. While there was no clear decline in residues for these samples from 0 to 3 DALA, residues did decline in the samples collected at later dates for this application rate.

In terms of the residue definition for enforcement purposes much lower residues were observed. At the proposed 3 day withholding period after the last of 3 applications at 96 g ai/ha (1× proposed rate) residues of parent plus enol in parent equivalents were <0.045 and 0.07 mg/kg.

Cabbage

Six trials were conducted on cabbage grown in Tasmania, Queensland, South Australia and Victoria in 2005/06. Three applications of a 240 SC formulation of spirotetramat were made at 48, 96 or 144 g ai/ha at weekly intervals just prior to crop maturity. Spray volumes ranged from 500 – 626 L/ha. Samples were collected nominally at 7 days after the second application and at 0, 3, 7 and 14 days after the third application.

Total spirotetramat residues in cabbage immediately before the 3rd application at 96 g ai/ha (1× proposed rate) were <0.11 (n = 2), 0.16, 0.21, 0.35 and 3.61 mg/kg. Immediately after the 3rd application at this rate residues were <0.11, 0.20, 0.28. 0.80, 1.12 and 2.91 mg/kg. This suggests the residue of 3.61 mg/kg before the 3rd application may be an outlier. At the proposed 3 day WHP after the last application at 96 g ai/ha residues were <0.11, 0.14, 0.25, 0.36, 0.60 and 1.36 mg/kg. A clear decline in residues was not observed for samples collected at later dates. For example, the residue of 1.36 mg/kg increased to 1.86 mg/kg at 7 days after the last application at the proposed rate. However, this residue declined in a sample taken 14 DALA.

Maximum total spirotetramat residues observed in cabbage at 3 or more days after application at 96 g ai/ha were <0.11, 0.16, 0.34, 0.50, 0.60 and 3.61 mg/kg.

In terms of the residue definition for enforcement, the maximum residues of parent + enol in cabbage at 3 or more days after the last application at 96 g ai/ha were <0.045, 0.057, 0.12, 0.37, 0.38 and 3.37 mg/kg.

Broccoli

Four residue trials were conducted on broccoli at Werribee South, Victoria and Gatton, Queensland in 2005/06. Three applications of a 240 SC formulation of spirotetramat were made at weekly intervals at 48, 96 or 144 g ai/ha just prior to crop maturity. Spray volumes ranged from 510 – 904 L/ha. Samples of broccoli were collected nominally at 7 days after the 2nd application and at 0, 1, 3, 7 and 14 days after the 3rd application.

Total residues of spirotetramat immediately before the 3rd application at 96 g ai/ha (1× proposed rate) were 0.24, 0.74, 0.76 and 1.11 mg/kg. Immediately after the 3rd application at this, rate residues were 0.76, 1.05, 1.47 and 2.47 mg/kg indicating that a significant proportion of the residue was due to the earlier applications. At the proposed 3 day withholding period after the last application at 96 g ai/ha (1× proposed rate) total residues were <0.11, 0.65, 1.02 and 1.72 mg/kg. A decline in residues was not observed for samples collected at 7-8 days after the last application at this rate when residues of 1.38, 1.46 and 3.77 mg/kg were detected. Residues tended either to decline again or at least stay at similar levels in trials where samples were collected out to 10 – 14 DALA.

Maximum total spirotetramt residues in broccoli at 3 or more days after application at 96 g ai/ha were 0.24, 1.38, 1.46 and 3.77 mg/kg.

In terms of the residue definition for enforcement, the maximum residues of parent + enol in broccoli at 3 or more days after application at 96 g ai/ha were <0.045, 0.13, 1.25 and 3.40 mg/kg.

Summary of Australian data

In terms of the residue definition for dietary exposure, total spirotetramat residues in Brassica vegetables at 3 or more days after the last application at 96 g ai/ha (1× proposed rate) in Australian trials were:

Brussels sprouts – 0.48 and 0.83 mg/kg.
Cabbage – <0.11, 0.16, 0.34, 0.50, 0.60 and 3.61 mg/kg.
Broccoli – 0.24, 1.38, 1.46 and 3.77 mg/kg.

If just the enforcement residue definition of parent plus the enol metabolite is considered then residues in Brassica vegetables at 3 or more days after the last application at 96 g ai/ha in the Australian trials were:

Brussels sprouts – <0.045 and 0.07 mg/kg.
Cabbage – <0.045, 0.057, 0.12, 0.37, 0.38 and 3.37 mg/kg.
Broccoli – <0.045, 0.13, 1.25 and 3.40 mg/kg.

Overseas data

The Australian residue data was supported by data from 15 European and 15 US trials.

In the European trials, total spirotetramat residues in Brassica vegetables at 3 or more days after the last of 3 applications at 72 g ai/ha (0.75× proposed rate) were:

Broccoli and cauliflower - 0.241, 0.260, 0.320, 0.427, 0.521 and 0.578 mg/kg.
Brussels sprouts - 0.088, 0.106, 0.131 and 0.218 mg/kg.
Cabbage - 0.091, 0.097, 0.104, 0.107 and 0.232 mg/kg.

In terms of the enforcement residue definition, maximum residues of parent plus the enol metabolite in these trials were:

Broccoli and cauliflower - 0.065, 0.14, 0.16, 0.27, 0.33 and 0.37 mg/kg.
Brussels sprouts - 0.051, 0.063, 0.079 and 0.14 mg/kg.
Cabbage - 0.027, 0.047, 0.066, 0.072 and 0.20 mg/kg.

In the US trials, total residues of spirotetramat in Brassica vegetables at 3 or more days after the last of 2 applications at 88 gai/ha (0.92× proposed rate) were:

Broccoli/cauliflower – 0.178, 0.226, 0.314, 0.446, 0.542, 0.548, 0.835 and 0.871 mg/kg.
Cabbage – 0.056, 0.067, 0.192, 0.241, 0.319, 0.449 and 0.515 mg/kg.

In terms of the enforcement residue definition, maximum residues of parent plus the enol metabolite in these trials were:

Broccoli/cauliflower – 0.076, 0.095, 0.101, 0.104, 0.211, 0.280, 0.309 and 0.394 mg/kg.
Cabbage – 0.020, 0.023, 0.077, 0.152, 0.193, 0.210 and 0.233 mg/kg.

MRL recommendation

An MRL of 7 mg/kg for spirotetramat on VB 0040 Brassica (cole or cabbage) vegetables, Head cabbages, Flowerhead brassicas [except Brussels sprouts] is appropriate based on the Australian data. A separate MRL of 1 mg/kg is recommended for spirotetramat on VB 0402 Brussels sprouts to cover the lower residues detected in this crop. With respect to the proposed 3 day withholding period it is noted that the highest residue was often observed at 7 days after the last application rather than 3. However, as residues at 7 DALA were still within the proposed MRL it is considered that a 3 day WHP is acceptable.

The highest total spirotetramat residues for dietary exposure assessment were 3.77 mg/kg for VB 0040 Brassica (cole or cabbage) vegetables, Head cabbages, Flowerhead brassicas [except Brussels sprouts] and 0.83 mg/kg for VB 0402 Brussels sprouts.

Animal Commodity MRLs

Brassicas are not a major animal feed. Use of the product on Brassicas grown for forage or fodder is prohibited as a label restraint. Grazing of other Brassica vegetables is not common practice, with vegetables unlikely to exceed more than 5% of an animal's diet on a dry matter basis. Feeding of Brassica vegetables with a HR of 3.77 mg/kg and dry matter content of 15% would correspond to a maximum spirotetramat intake of 1.26 ppm in the feed if feeding occurred at the 5% limit. An animal transfer study suggests feeding at this level would result in residues at the LOQ (0.01 mg/kg) for kidney and below the LOQ in other tissues and milk. The following animal commodity MRLs are recommended for spirotetramat:

MO 0105	Edible offal (mammalian)	0.05 mg/kg
MM 0095	Meat (mammalian)	*0.01 mg/kg
ML 0106	Milks	*0.005 mg/kg

ESTIMATED DIETARY INTAKE

The chronic dietary exposure to spirotetramat is estimated by the National Estimated Daily Intake (NEDI) calculation encompassing all registered/temporary uses of the chemical and the mean daily dietary consumption data derived from the 1995 National Nutrition Survey of Australia. The NEDI calculation is made in accordance with WHO Guidelines[1] and is a conservative estimate of dietary exposure to chemical residues in food. The NEDI for spirotetramat is equivalent to 2.5% of the ADI.

It is concluded that the chronic dietary exposure of spirotetramat is acceptable and residues in food will not pose an undue hazard to the safety of people.

The acute dietary exposure is estimated by the National Estimated Short Term Intake (NESTI) calculation. The NESTI calculations are made in accordance with the deterministic method used by the JMPR with 97.5th percentile food consumption data derived from the 1995

1.Guidelines for predicting dietary intake of pesticide residues, WHO, 1997.

National Nutrition Survey of Australia. NESTI calculations are conservative estimates of acute exposure (24 hour period) to chemical residues in food.

The acute exposure to spiroteramat residues in Brassica vegetables is considered acceptable, ranging from 0 to 14.6% of the ARfD for children (2-6 years) and from 0 to 5.5% of the ARfD for the general population (2+ years).

Bioaccumulation potential

Spirotetramat has a K_{ow} log P of 2.51 (pH 7) indicating low fat solubility. In the goat metabolism study the TRR in subcutanaeous fat was at a similar levels to those in muscle, while the TRRs of omental and perirenal fat were significantly lower. In the hen metabolism study the TRRs in fat and muscle were at similar levels. A dairy cattle transfer study confirmed that there was no preferential accumulation of spirotetramat residues in fat and highest residues were observed in kidney. In addition there was no concentration of residues in milk fat separated from whole milk.

Spray Drift

The draft label includes the following statement in relation to spray drift:

'DO NOT apply under weather conditions or from spraying equipment that may cause spray drift onto nearby crops/plants, cropping lands or pastures.'

The potential for residues in livestock as a result of spray drift from both ground and aerial application has also been considered In an animal transfer study provided with the application, the maximum residue in dairy cattle after dosing with spirotetramat at 3 ppm was 0.025 mg/kg in kidney. The maximum feeding level for residues in kidney to be at the LOQ (0.01 mg/kg) is therefore 1.2 ppm. Assuming pasture contains 1500 kg dry matter per hectare this would correspond to a maximum drift of 1.8 g ai/ha. Calculations using AgDisp for aerial application and AgDrift for ground application indicate that the following no spray zones are appropriate to ensure that there are no detectable residues in livestock as a result of spray drift.

For Aerial Application	
Wind Speed Range at Time of Application	Downwind No-Spray Zone
3 to 8 kilometres per hour	100 metres
9 to 14 kilometres per hour	120 metres
15 to 20 kilometres per hour	160 metres
For Ground Application	
Wind Speed Range at Time of Application	Downwind No-Spray Zone
3 to 20 kilometres per hour	10

RECOMMENDED AMENDMENTS TO MRL STANDARD

The following MRLs will be established:

Table 1

Compound	Food		MRL (mg/kg)
ADD: Spirotetramat	VB 0040	Brassica (cole or cabbage) vegetables, Head cabbages, Flowerhead brassicas [except Brussels sprouts]	7
	VB 0402	Brussels sprouts	1

	MO 0105	Edible offal (mammalian)	0.05
	MM 0095	Meat (mammalian)	*0.01
	ML 0106	Milks	*0.005

Table 3

Compound	Residue
ADD: Spirotetramat	For enforcement: Sum of spirotetramat, and cis-3-(2,5-dimethylphenyl)-4-hydroxy-8-methoxy-1-azaspiro[4.5]dec-3-en-2-one, expressed as spirotetramat. Commodities of plant origin for dietary exposure assessment: Sum of spirotetramat, cis-3-(2,5-dimethylphenyl)-4-hydroxy-8-methoxy-1-azaspiro[4.5]dec-3-en-2-one, cis-3-(2,5-dimethylphenyl)-3-hydroxy-8-methoxy-1-azaspiro[4.5]decane-2,4-dione, cis-3-(2,5-dimethylphenyl)-4-hydroxy-8-methoxy-1-azaspiro[4.5]decan-2-one and the glucoside of cis-3-(2,5-dimethylphenyl)-4-hydroxy-8-methoxy-1-azaspiro[4.5]dec-3-en-2-one, expressed as spirotetramat. Commodities of animal origin for dietary exposure assessment: Sum of spirotetramat, cis-3-(2,5-dimethylphenyl)-4-hydroxy-8-methoxy-1-azaspiro[4.5]dec-3-en-2-one and the glucuronic acid conjugate of cis-3-(2,5-dimethylphenyl)-4-hydroxy-8-methoxy-1-azaspiro[4.5]dec-3-en-2-one, expressed as spirotetramat.

WITHHOLDING PERIODS

The following withholding period is required in relation to the above MRLs:

Harvest (H)

Brassicas: DO NOT harvest for 3 days after application

Commodities exported

Brassica vegetables are not considered major export commodities[2] and the overall risk to export trade is considered to be small. Details of export volumes, values and markets are summarised below. [3]

Destination and Value of Exports

Broccoli

In 2002/03 Australia exported 6,428 tonnes of broccoli valued at $13,310,000. The major export markets were Singapore (2,764 tonnes), Malaysia (1,399 tonnes) and Japan (770 tonnes).

Brussels sprouts

In 2002/03 Australia exported 653 tonnes of Brussels sprouts valued at $829,000. The major export markets were the Netherlands (451 tonnes), New Zealand (108 tonnes) and the United Kingdom (40 tonnes).

Cabbage

In 2002/03 Australia exported 1,913 tonnes of cabbage valued at $1,918,000. The major export markets were Japan (508 tonnes), Taiwan (419 tonnes) and Singapore (322 tonnes).

Cauliflower

In 2002/03 Australia exported 16,567 tonnes of cauliflower valued at $23,409,000. The major export markets were Malaysia (10,200 tonnes), Singapore (5,360 tonnes) and Hong Kong (369 tonnes).

CODEX ALIMENTARIUS COMMISSION AND OVERSEAS MRLS

The Codex Alimentarius Commission (Codex) is responsible for establishing Codex Maximum Residue Limits (CXLs) for pesticides. Codex CXLs are primarily intended to facilitate international trade, and accommodate differences in Good Agricultural Practice (GAP) employed by various countries. Some countries may accept Codex CXLs when importing foods. Spirotetramat has not been considered by Codex.

Overseas residue MRLs/tolerances for spirotetramat have yet to be established. However, proposed US MRLs for spirotetramat have been published as an SPS (Sanitary and Phytosanitary) notification by the World Trade Organisation. Canada has also proposed MRLs at the same level. The following table summarises the proposed US and Canadian MRLs for Brassicas and animal commodities:

Commodity	Proposed US MRL (mg/kg)
Brassica, head and stem, subgroup 5A	2.5
Brassica, leafy greens, subgroup 5B	8.0
Milk	0.01
Cattle, meat	0.02

[2] Part 5B of the Vet Requirements Series and Ag Requirements Series, Overseas Trade Aspects of Residues in Food Commodities, August 2004.

[3] The Australian Horticulture Statistics handbook 2004.

Cattle, fat	0.02
Cattle, meat by products	0.02

It is noted that the proposed US and Canadian residue definition for commodities of plant origin is spirotetramat and its metabolites BYI 08330-enol, BYI 08330-ketohydroxy, BYI 08330-enol-Glc and BYI 08330-monohydroxy. For animal commodities the proposed US and Canadian (enforcement) definition is spirotetramat and its metabolite BYI 08330-enol.

POTENTIAL RISK TO TRADE

Export of treated produce containing finite (measurable) residues of spiroteramat may pose a risk to Australian trade in situations where (i) no residue tolerance (import tolerance) is established in the importing country or (ii) where residues in Australian produce are likely to exceed a residue tolerance (import tolerance) established in the importing country.

Residues are expected to occur in Brassicas and export markets have not established MRLs or import tolerances, creating a potential risk to trade. The following export advice is included on the draft labels to mitigate this risk:

'Growers should note that MRLs or import tolerances do not exist in all markets for edible produce treated with Movento 240 SC. If you are growing edible produce for export, please check with Bayer CropScience Pty Ltd for the latest information on MRLs and import tolerances before using Movento 240 SC'.

With respect to trade in animal commodities, detectable residues are not expected to occur in the meat, fat or milk of livestock that have been fed treated Brassica vegetables. The maximum predicted residue in kidney would be at the LOQ (0.01 mg/kg). As detectable residues are unlikely and as the livestock industry has mechanisms in place through National Vendor Declarations to determine if stock have been exposed to processed vegetable wastes in the 60 days prior to sale the overall risk to export trade in animal commodities is considered to be low.

Conclusions

Quantifiable residues of spirotetramat are likely to occur in Brassicas when Movento 240 SC Insecticide is used as directed. This creates a potential risk to trade as there are currently no established overseas MRLs for spiroteramat. In this situation, use of the product is not recommended in the production of crops destined for export.

Comments are sought on the potential for Movento 240 SC Insecticide to unduly prejudice Australian export trade when used on Brassica crops to control Silverleaf Whitefly.

Health hazards

Spirotetramat has low acute oral, dermal and inhalation toxicity. It is non-irritating to the skin but a severe irritant to the eyes and exhibits a skin sensitisation potential under the conditions of the guinea pig maximization test and the local lymph node assay, but not the Buehler patch test. In addition, Spirotetramat can potentially induce impaired fertility in humans and could be a substance with possible risk of harm to the unborn child.

Spirotetramat is not on the NOHSC *Hazardous Substances Information System* (HSIS) (NOHSC, 2005). Based on the toxicology information provided, the OCS classified spirotetramat as a hazardous substance according to NOHSC *Approved Criteria for Classifying Hazardous Substances* (NOHSC, 2004), with the following risk phrases:

R36	Irritating to eyes
R43	May cause sensitisation by skin contact
R62	Possible risk of impaired fertility
R63	Possible risk of harm to the unborn child

The following cut-off concentrations apply for spirotetramat:

Conc. ≥ 20%	R36
Conc. ≥ 1%	R43
Conc. ≥ 5%	R62
Conc. ≥ 5%	R63

Movento 240 SC Insecticide has low acute oral, dermal and inhalational toxicity. It is a slight eye irritant with skin sensitisation potential. Based on toxicology information of the product and active ingredient, Movento 240 SC Insecticide is classified as a hazardous substance in accordance with NOHSC Approved Criteria for Classifying Hazardous Substances (NOHSC, 2004) with the following risk phrases:

R36	Irritating to eyes
R43	May cause sensitisation by skin contact
R62	Possible risk of impaired fertility
R63	Possible risk of harm to the unborn child

Selection of a NOEL for OH&S risk assessment

Occupational exposure to Movento 240 SC Insecticide is most likely to occur via the dermal and inhalational routes, when spray drift or the concentrated product comes into contact with a worker's skin, or spray mist is inhaled. Therefore, a NOEL from a repeat-dose, long-term, dermal or inhalational study is most appropriate for use in the OH&S risk assessment. However those route-specific studies are not available for spirotetramat with appropriate exposure times. Therefore, a No Observable Effect Level (NOEL) values from dietary studies are considered for OH&S risk assessment. In the Occupational Health and Safety (OH&S) dossier, the applicant used a NOEL of 10 mg/kg bw/d, derived from a rabbit developmental toxicity study for OH&S risk assessment which is not considered to be appropriate from the viewpoint of the OCS. A NOEL of 5 mg/kg bw/d, derived from a one-year dog study, is the lowest NOEL for spirotetramat, reported in the public health assessment summary.

Based on the use pattern of the product, the NOEL of 5 mg/kg bw/d from this one-year dog study is considered appropriate for the OH&S assessment. Since the oral absorption rate of spirotetramat across the GI tract is above 90%, a correction for 'internal dose' is not necessary for this risk assessment.

The assessment for appropriate safety directions required for the proposed label took into account also the reproductive and developmental endpoints (420 and 1000 mg/kg bw/day respectively). Given the endpoints recognised from the one-year dog study of decreased serum T3 and T4 levels, increased incidence of brain dilation and thymus involution at the next higher dose 20 mg/kg bw/day, are much more sensitive than those mentioned above, the NOEL selected above will address these risks. Consequently, it is considered that the safety directions developed for protection of the risk of thymus toxicity and brain dilation, will mitigate risks that may occur at does much higher than 5 mg/kg bw/day, such as reproductive and developmental toxicity.

Safety directions required:
May irritate the eyes. Repeated exposure may cause allergic disorders. Avoid contact with eyes and skin. When opening the container and preparing spray, wear cotton overalls buttoned to the neck and wrist (or equivalent clothing) and elbow length chemical resistant gloves. If product on skin immediately wash area with soap and water. If product in eyes wash it out immediately with water. Wash hands after use. After each day's use, wash gloves and contaminated clothing.

Formulation, packaging, transport, storage and retailing

Movento 240 SC Insecticide will be formulated overseas and imported into Australia in 1, 5 and 10L High Density Polyethylene containers, ready for sale. Transport workers and store persons will handle the packaged product and could only become contaminated if packaging were breached.

Use pattern

Movento240 SC Insecticide is intended for silverleaf whitefly in Brassica vegetables and will be applied by spraying using open or enclosed cab tractor-mounted or drawn sprayer fitted with hydraulic nozzles. The product will be applied at a rate of 400 mL product/ha (96 g ai/ha) with three applications per season at intervals of at least 7 days.

According to the applicant, areas treated per work-day will be 20 ha. Therefore, a worker could apply up to 8 L of product (1.92 kg a.i.) per day for tractor mounted or drawn spray application. It will potentially be used as an insecticide spray for up to a total of 6 months per year.

According to the applicant, post-application activities such as crop inspection, pruning and harvesting could be required which may lead to worker exposure.

The following withholding period has been recommended on the draft label and is relevant to re-entry considerations:

Brassica vegetables: Do not harvest for 3 days after application

Exposure during use

Farmers and their employees, and professional applicators, will be the main users of the product. Contract workers will be exposed to the product repeatedly. Workers may become contaminated with the product/spray during mixing/loading, spraying, cleaning up spills and maintaining equipment. The main routes of exposure to the product will be dermal and inhalation although ocular exposure is also possible.

There are no worker exposure studies on spirotetramat or Movento 240 SC Insecticide available for assessment. In the absence of worker exposure data, the applicant used UK Predictive Operator Exposure Model (POEM) to estimate worst-case worker exposure (based on maximum product use according to the Australian use pattern = 1.92 kg spirotetramat) during mixing/loading and application. For comparative purpose, OCS used the Pesticide Handler Exposure Database (PHED) Surrogate Exposure Guide (1998) to estimate the worker exposure to spirotetramat using the same maximum working rate.

These estimations in conjunction with toxicology data demonstrated that the use of elbow-length chemical resistant gloves in conjunction of wearing cotton overalls buttoned to the neck and wrist are required to protect workers when opening the container and preparing spray.

Exposure during re-entry

Workers entering treated areas can be exposed to product residues during crop management activities. In the absence of re-entry worker exposure data, the applicant estimated post application dermal exposure to spirotetramat for workers undertaking crop management activities, utilising activity specific transfer co-efficients (TC) in conjunction with dislodgeable foliar residue (DFR) data. An exposure value of 13.5 µg/kg/day is estimated from exposure immediately after application and a MOE of 740 for re-entry was indicated by the applicant. However the re-entry MOE provided by the applicant is underestimated by approximately 5 times from the viewpoint of the OCS. The adjusted MOE is 148, which is over the required value of 100.

Considering the likely risks to workers during re-entry, a re-entry statement is recommended until the spray has dried.

Recommendations for safe use

Users should follow the instructions and Safety Directions on the product label. Safety Directions include the wearing of cotton overalls buttoned to the neck and wrist and use of elbow-length chemical resistant gloves when opening the container and preparing spray.

The PPE recommended should meet the relevant Australian Standards.

Re-entry Statement

"Do not allow entry into treated areas until the spray has dried, unless wearing cotton overalls buttoned to the neck and wrist (or equivalent clothing) and chemical resistant gloves. Clothing must be laundered after each day's use."

Conclusion

The registration of spirotetramat at 240 g/L in Movento 240 SC Insecticide, as a suspension concentrate (SC) formulation for control of silverleaf whiteflies on various brassica vegetable crops is supported.

Movento 240 SC Insecticide can be used safely if handled in accordance with the instructions on the product label and any other control measures described above. Additional information is available on the product MSDS.

ENVIRONMENTAL FATE

Hydrolysis

The hydrolytic stability of radiolabelled spirotetramat was investigated in dark, sterile buffer solutions at pH 4, 7 and 9. Spirotetramat was shown to hydrolyse with strong dependence of pH, with DT50 values at 25°C of 32.5, 8.6 and 0.32 days at pH 4, 7 and 9, respectively. Hydrolysis was also temperature dependent, increasing with increasing temperature. No volatiles were formed as confirmed by the complete mass balance. The hydrolytic degradation of spirotetramat resulted in the formation of spirotetramat-enol as the only major metabolite, which was shown to be stable under conditions of sterile hydrolysis (pH 4, 7 and 9 at 25 and 50°C) in a separate study.

Aqueous photolysis

The aqueous phototransformation of radiolabelled spirotetramat was investigated at 25°C in sterile buffer solutions at pH 5.0 and in sterilised natural water at pH 7.9. Following 7 days continuous simulated irradiation of the buffer solution, spirotetramat degraded (following SFO kinetics) with a half-life of 2.7 days and a DT90 of 9.0 days, increasing to 3 and 10 days, respectively, following correction for hydrolysis. The uncorrected half-life corresponds to 12.0, 9.3 and 11.4 days under environmental midday summer light in Athens (Greece), Phoenix (USA) and Edmonton (Canada). Spirotetramat degraded (via photo-rearrangement) in the buffer to 4 major degradation products, namely spirotetramat-photo-cyclopentyl, spirotetramat-photo-hydroxymethyl, spirotetramat-photo-formyl and spirotetramat-photomethyl carbonate, at maximum amounts of 42.9, 22.9, 11.5 and 19.3% of AR, respectively. These metabolites did not significantly decrease during the study period. Slower degradation (DT50 of 26.2 days) was observed in the dark controls, with only the common hydrolysis product spirotetramat-enol observed. The photodegradation of spirotetramat can be also considered a significant route for the elimination of the compound from the environment under acidic conditions.

Following 10 days continuous irradiation in sterilised natural water, spirotetramat extensively degraded (following SFO kinetics) with a half-life of 0.19 days and a DT90 of 0.63 days, increasing to 0.22 and 0.71 days, respectively, following correction for hydrolysis. The uncorrected half-life corresponds to 0.66, 0.50 and 0.62 days under environmental midday summer light in Athens (Greece), Phoenix (USA) and Edmonton (Canada). Spirotetramat degraded to spirotetramat-enol (maximum 81.9% of AR at 1 DAT and declining rapidly thereafter), methoxy-cyclohexyl-aminocarboxylic acid (maximum 11.3 % of AR at study termination) and methoxy-cyclohexanone (17.5% of AR), however, no photo-rearrangement products were formed. Under dark conditions only spirotetramat-enol was formed owing to hydrolysis. Slower degradation (DT50 of 1.5 days) was observed in the dark controls, with only the common hydrolysis product spirotetramat-enol observed. The photodegradation of spirotetramat can be also considered a significant route for the elimination of the compound from the environment under more alkaline conditions. This study demonstrates that photo-rearrangement products are not likely to form under more natural and alkaline conditions. Although the likelihood of these products occurring in more acidic natural surface waters remains unclear, the rapid half-life of spirotetramat in water/sediment systems (pH 6.7 and 7.2) of ~ 0.8 days indicates that significant formation of these products is highly unlikely to occur.

In two separate studies, the quantum yields of the direct photochemical degradation of spirotetramat and spirotetramat-enol were investigated in sterile, unbuffered water (pH 6.2-6.4 for former; unspecified for the latter) using a mercury immersion lamp (> 295 nm) and a uranyl oxalate actinometer. Mean DT50 values were 0.15 and 1.39 days for the parent and

enol, respectively. No dark control samples were investigated, however, no significant hydrolysis is expected over the testing period of 4 hours. The quantum yield for the parent and enol were calculated to be 0.00571 and 0.000252, respectively. The predicted environmental half-lives are 0.5 and 9 days, respectively, at 40°C in summer sunlight using the GC-SOLAR model, however, this increases to 1 and 16 days, respectively, using the Frank & Klöpffer model.

Soil photolysis

A soil photolysis study was conducted using 3- and 5-^{14}C labelled spirotetramat on one (moist) viable soil, but with a supplementary study (with sampling days 0 and 7 only) on the same soil when dry and on another moist soil. In the main study, spirotetramat degraded with a half-life of 2.4-5.0 days (depending on the label) compared with 0.6-1.2 days in the dark. The supplementary study indicated much slower photolysis and no degradation in the dark on the dry soil, but significantly faster degradation (similar to rate in the dark) in the moist soil.

It was not possible to assess the rate of photodegradation of spirotetramat on moist soil because most degradation was due to microbial activity (which was more active under dark conditions). Under dry conditions microbial activity was reduced and spirotetramat photodegraded, but the (supplemental) study had too few data points to calculate a half-life. In general, phototransformation on moist soil surfaces is not considered to significantly contribute to the overall dissipation of spirotetramat from the environment owing to the extremely rapid degradation under moist conditions. Four major transformation products (>10% of AR) were found in the irradiated soil samples, spirotetramat-enol, spirotetramat-ketohydroxy, 4-methoxy-cyclohexanone (only observable using [5-^{14}C] labelled parent) and dimethyl-benzoic acid (only observable using [3-^{14}C] labelled parent). The formation of the enol and ketohydroxy degradates was significantly higher in the dark samples. Minor transformation products determined were spirotetramat-glyoxylic amide and spirotetramat-enol dimer. 4-Methoxy-cyclohexanone and dimethyl-benzoic acid were not found in dark samples indicating that these metabolites are photolysis metabolites only. Given that dimethyl-benzoic acid was shown not to exceed 4.8% of AR in the outdoor metabolism study including natural sunlight, it is not considered a relevant photodegradate. A soil photolysis study on sterile soil is expected for submission by end of 2008.

In a separate degradation study (conducted due to label detection difficulties in the main study), the soil photolysis metabolite 4-methoxy-cyclohexanone was shown to degrade very quickly in all three tested soils under aerobic conditions. The DT50 and DT90 values were <1 day for all 3 soils, except for one soil with a DT90 value of 1.8 days. No major degradates were detected.

Aerobic soil metabolism

One aerobic soil metabolism laboratory study for each of spirotetramat, spirotetramat-enol and methoxycyclohexanone were presented in support of the application. An additional outdoor aerobic soil metabolism study was presented as a supporting study. The study using spirotetramat-enol as parent (using alkaline extraction) was conducted to overcome metabolite instability observed in the spirotetramat study during the acidic extraction procedure.

Under standard aerobic conditions (20°C), the metabolism of spirotetramat ([3-^{14}C] label) was studied in 3 EU soils (50 days) and one US soil (360 days) and shown to proceed via three pathways which all start with the hydrolytic cleavage of the spirotetramat ester into spirotetramat-enol. Spirotetramat degraded very quickly during the first day to <10% of AR in all soils, with no dependency on soil pH (over the range 4.7-6.8 $CaCl_2$) to form the enol and spirotetramat-ketohydroxy at maximum amounts of 24.3% (by 3 DAT) and 16.3% (by 1 DAT), respectively. The spirotetramat-enol dimers 1 and 2 were also detected at respective maximum levels of 12.7% (7 DAT) and 9.2% (30 DAT). The overall degradation pattern was

biphasic. Although a double first order in parallel (DFOP) kinetic model best fitted the data, this is not appropriate for most environmental models. Simple first-order (SFO) kinetics was the preferred model and showed good fit to initial degradation (close to the biphasic models), with a DT50 range of 0.08-0.33 days. The DT90 values were slightly underestimated compared to the range of 0.89-1.26 days obtained from the DFOP model.

Following the major degradation pathway, spirotetramat-enol is rapidly oxidized at the benzylic carbon position into spirotetramat-ketohydroxy which is hydrolytically opened into spirotetramat-MA-amide and finally mineralized into CO_2. In the study using spirotetramat-enol as parent ([3-^{14}C] and [5-^{14}C] label) and the same test soils as used in the parent degradation study, spirotetramat-ketohydroxy was observed at maximum amounts of 24.0% of AR (by 1 DAT), spirotetramat-MA-amide was observed at maximum amounts of 5.2% of AR by 7 DAT, and the dimers were present at up to 5% each. No other metabolite was observed > 5% of AR in this study. Spirotetramat-oxo-ketohydroxy and spirotetramat-desmethyl-enol, degradation products from an alternative pathway, were observed at <2% AR. The formation of dimers in the parent and enol degradation studies are considered an artificial process caused by hot-spot application, and thus are not considered environmentally relevant metabolites. Similar to the parent, spirotetramat-enol dissipated following pronounced biphasic kinetics, with an extremely quick first phase and a significantly slower second phase, explained by extensive oxidation to spirotetramat-ketohydroxy or extensive binding to the soil matrix with slow release contributing to the slower phase.

Assuming degradation of the mobile fraction of spirotetramat-enol follows simple first order-reverse binding (SFO-RB) kinetics, the degradation DT50 values of spirotetramat-enol ranged from 0.02–0.16 days and 10.9–40.9 days for the DT90 using a DFOP kinetic model. Applying the SFO-RB model to the degradation of spirotetramat-ketohydroxy yielded DT50 and DT90 value ranges of 1.5–16.7 and 5.1–55.6 days, respectively. Using the same approach, DT50 and DT90 values of spirotetramat-MA-amide in soil were 0.3–5.4 and 1.0–18.1 days, respectively. Degradation rates of spirotetramat-ketohydroxy and spirotetramat-MA-amide obtained from the more simplistic models closely represent those obtained from the higher tier approach, as expected from degradation almost exclusively attributed to the initial phase.

Formation of CO_2 in the spirotetramat degradation study was in a range of 9.7–19.4% of AR by 50 DAT in the EU soils, with an increase of 9.7 to 15.3% of AR from 50 to 360 DAT in the US soil. The soil with the highest content of microbial biomass showed the highest mineralisation rate. Formation of CO_2 in the spirotetramat-enol degradation study was in a range of 16.7–43.0% of AR by study termination (119 DAT). Significant higher $^{14}CO_2$ amounts were released from spirotetramat-enol labelled in the [3-^{14}C] position. In the spirotetramat study, the portion of non-extractable radioactivity (NER) rapidly increased during the first 3 days reaching a plateau concentration of ~22–35 % of AR. A similar but even more pronounced formation of NER was determined in the spirotetramat-enol study using a slightly alkaline extraction procedure. Immediately after application 4.2–28.4 % of AR was bound to the soil matrix, reaching a plateau concentration by 1 DAT of ~40–60 % of AR.

The biodegradation of [3-^{14}C] labelled spirotetramat (OD 100 formulation) was additionally investigated in two semi-disturbed (without sieving) soils kept in planting containers under outdoor climatic conditions (open system, protected from rainfall and exposed to natural temperature, humidity and light-dark cycles) considered more realistic for the intended use. In close agreement to the laboratory results, the parent compound was quickly degraded (SFO kinetics) with a DT50 of 1.2 and 2.9 days for the two tested soils, respectively. Three new metabolites (<5% of AR) were identified within this study (in comparison to the laboratory study): spirotetramat-glyoxylic amide, dimethyl-benzoic acid and spirotetramat-ketohydroxy-carboxy. The spirotetramat-enol dimers were detected at ≤1.5 % of AR after broadcast application of the product. Maximum formation of NER was distinctly lower than observed in the laboratory studies with 16.8% of AR by 63 DAT and decreasing thereafter, indicating an

enhanced overall degradation of the parent and its metabolites in soil under real outdoor conditions in comparison to the laboratory degradation studies.

Anaerobic soil metabolism

Anaerobic soil metabolism was studied in one soil, with a very short aerobic phase of 4.8 h before converting to anaerobic conditions. Although the redox potential and dissolved oxygen content were said to be measured in the latter, it is not clear when these measurements were taken as no values have been tabulated in the OECD monograph. However, anaerobic bacteria plate count tests are said to have indicated that the soil was anaerobic viable throughout this phase.

The degradation pathway is almost identical to the degradation pathway obtained in aerobic soil. In a flooded soil study over 180 days it was shown that spirotetramat declines quickly, with a first-order multi compartment (FOMC) kinetic model (showing the best visual fit – r^2 = 0.993) yielding entire system DT50 and DT90 values of 0.06 and 1.33 days, respectively. The detected metabolites were almost identical to those formed upon the aerobic transformation in the aerobic metabolism study. Spirotetramat-enol and spirotetramat ketohydroxy were the major metabolites present at 54.6 (DAT 180) and 19.4% (DAT 1) of AR in the entire system. Spirotetramat-MA-amide reached levels >5% of AR towards the end of the study and appeared to be increasing. The minor metabolite spirotetramat-di-hydroxy was not observed in the aerobic soil study, but was formed in the aerobic aquatic metabolism study. Therefore it can be excluded that this metabolite will be specially formed under anaerobic conditions.

Aerobic aquatic metabolism

The aerobic biotransformation of C^{14}-radiolabelled (3' and 5' positions) spirotetramat was studied in two contrasting dark natural pond water/sediment systems, including a loam sediment system (organic carbon 4.4%, water pH of 6.7 and a sediment pH in $CaCl_2$ of 5.6), and a loamy sand sediment system (organic carbon 0.99%, water pH of 7.2 and a sediment pH in $CaCl_2$ of 6.8). The microbial activity in the former was 3.5× higher. Over 120 days, material balances for the total systems were 94.4-102.6% of AR. Aerobic conditions were assured in water (>350 mV) and in sediment were, at worst, slightly anaerobic (>42 mV). However, tabulated results in the monograph contradict the text, with negative redox values recorded in the former for sediment. Mineralisation of spirotetramat to $^{14}CO_2$ and the formation of non-extractable residues increased from negligible levels at 1 DAT to 5.9-24% and 32.6-40.7% of AR, respectively. Initial concentrations of spirotetramat in the water column and sediment were 70.2-82.4% and 1.4-2.2 of AR, respectively, and rapidly declined to undetectable levels in both phases by 7 DAT. Movement of spirotetramat to sediment was observed briefly over the first day, with a maximum occurrence of 3.4% of AR% by 1 DAT.

The major transformation products (> 10 % of AR) detected in water were spirotetramat-enol (maximum concentration of 77.4-79.7% of AR at 7 DAT, decreasing thereafter) and spirotetramat-ketohydroxy (maximum concentration of 17.4% of AR at study termination). Spirotetramat-enol moved to sediment over 14-60 days, reaching maximum concentrations of 15.5-41.2% of AR in this phase, and declining thereafter. Movement of the enol to sediment was more rapid, and higher concentrations reached, in the loam sediment system. Spirotetramat-ketohydroxy was undetectable in sediment for 7-14 days in the loam sediment, increasing thereafter to 12.9-42.8% of AR by study termination, but was detected within 3 days in the sandy loam sediment, reaching a maximum concentration of 31.4% AR by 120 DAT. Minor metabolites including spirotetramat-MA-amide, spirotetramat-oxo-enol isomer, spirotetramat-di-hydroxy and an unidentified peak were detected at 5-10% of AR.

Spiroetramat dissipated (following SFO kinetics) in the water column and whole system with DT50 and DT90 values of ~1 and ~3.3-3.5 days, respectively. Based on a supplemental study, spirotetramat dissipated from the water column and whole system with DT50 and DT90

values of ~0.8 and 2.6 days, respectively. Dissipation was slightly faster in the low organic matter sandy loam system. Based on multi-compartment modelling, degradation of spirotetramat-enol was slower, with mean DT50 and DT90 ranges of 37.9-59.0 and 126-196 days, respectively, in the entire system. The slower degradation of spirotetramat-enol in aquatic systems is due to that it degrades primarily via surface catalysed oxidation, and is supported by the stability of the enol in the anaerobic water/sediment study. Spirotetramat-ketohydroxy was considered to be stable in both systems.

Anaerobic aquatic metabolism

The anaerobic transformation of radiolabelled spirotetramat was studied over 120 days in a dark anaerobic water/sediment system, using a clay loam with a pH of 7.1 ($CaCl_2$) and an organic carbon content of 0.7%. The average redox potential was +25 mV (+55 mV at start to -20 mV after 120 days) in water and +15 mV (+68.5 mV at start to -38.5 mV after 120 days) in the sediment, confirming that anaerobic conditions were maintained in accordance with OECD TG 308. Material balances for the total systems were 90.1-102.2% of AR. Mineralisation and the formation of non-extractable residues were negligible.

Spirotetramat degraded rapidly from its 0 DAT concentrations of 81.3% of AR in the water column and 9.3% of AR in sediment to undetectable levels by 14 and 9 DAT, respectively. In both phases, the parent was completely transformed into the major metabolite spirotetramat-enol, which was stable in the water column, reaching 80.5% of DAT by 14 DAT and maintaining a concentration >71.7% for the remainder of the study. The metabolite partitioned to sediment at a maximum concentration of 28.5% of AR by 21 DAT, and was also stable in this phase, maintaining a concentration >23.1 % of AR for the remainder of the study.

The DT50 and DT90 values for spirotetramat in the water column and entire system were both calculated to be 2.8 and 9.3 days, respectively.

Dissipation studies

Four field dissipation studies (including bare and cropped soils) were conducted over 542 days with spirotetramat applied on a range of soil types in the USA, representing worst-case scenarios with respect to degradation (0.2-0.75% organic carbon in the top 15 cm of soil) and leaching behaviour (sandy soils with <10% clay). Spirotetramat as a 100 OD oil dispersion formulation was broadcast spray applied once at 439 g ac/ha in each study.

Under field conditions spirotetramat rapidly dissipated to undetectable levels within 7-14 days, with DT50 and DT90 ranges of 0.3–1.0 and 1.1-3.5 days (good fit to SFO kinetic model with r^2 >0.93). Since almost no transfer of spirotetramat into soil layers below 15 cm was observed and volatilisation is considered to be minimal (vapour pressure 5.6×10^{-9} Pa), dissipation of spirotetramat was considered more or less consistent with degradation. No differences were observed between bare ground and cropped plots. Owing to the short half-life of spirotetramat in soil, the potential for accumulation from one year to the next is not expected.

The major transformation products detected were spirotetramat-enol and spirotetramat-ketohydroxy, at maximum parent equivalent levels ranging from 15-57% and 30-61% of Day 0 total residue levels, respectively, in bare soil plots. In cropped plots, the respective levels ranged from 12-30% and 37-68%. Quantification of individual metabolite residues was strongly affected by the low storage stability of the former, which extensively degrades (as demonstrated in soil storage experiments) to the latter and is also strongly sequestered to the soil as non-extractable residues, even under frozen storage conditions. Given that the decline of spirotetramat-enol was most pronounced during the first 30 days of storage, residues of the 2 metabolites are likely to be under- or overestimated. Therefore, the kinetics of the combined residues of spirotetramat-enol and spirotetramat-ketohydroxy were evaluated. These

combined residues were found to have a DT50 range of 4.4–31.6 days and a DT90 range of 15.4–105 days, calculated using SFO kinetics. Again, no significant differences were found between bare ground and cropped plots. Total combined residues (also including spirotetramat and spirotetramat-MA-amide) were found to dissipate with DT50 and DT90 ranges of 5.0–23.4 and 16.7-77.8 days, resepctively. Potential of carry over of any residue from one year to the other year is considered minimal.

Residues of spirotetramat did not move below the surface layer (0–15 cm) in all sites, except Florida where residues of spirotetramat-enol and spirotetramat-ketohydroxy were detected above the LOQ (5 ppb) in the 15–30 cm layer between 1-7 DAT. It should be noted that the Florida test site represents worst-case conditions with heavy rainfall, very light soil (95 % sand in the top layer) and low organic matter (0.2%). Based on field dissipation data, leaching and groundwater contamination is unlikely to occur following application of spirotetramat.

Soil mobility

Spirotetramat

The adsorption/desorption characteristics of radiolabelled spirotetramat were determined in batch equilibrium experiments with 5 different soils (pH 4.7–6.8, organic carbon 0.7–2.4% and clay 7–28%). Since significant degradation of the test item was observed in a pre-test, the main test was performed with sterilised soil (using mercuric(II)chloride) and the equilibrium time was restricted to 3 h. For the adsorption phase, Freundlich adsorption coefficient (K_F) values ranged from 3.70-4.79 mL/g, and the corresponding K_{FOC} values ranged from 159-435 mL/g. Linear adsorption constants (K_d and K_{OC}) were close to the K_{OC} and K_{FOC} with ranges of 3.58-5.52 and 184–437 mL/g, respectively. The Freundlich exponent (1/n) ranged from 0.823-1.042, indicating that adsorption is not dependent on concentration of the test substance. Following one round of desorption, the K_F values ranged from 14.2-40.7 mL/g, and the corresponding K_{FOC} values ranged from 610-3606 mL/g. The 4-8× higher desorption coefficient values indicate strong binding of spirotetramat once adsorbed to the soil. Based on these values, spirotetramat is classified as of medium mobility according to the classification scheme of McCall *et al.* (1980).

Spirotetramat metabolites

The adsorption behaviour of spirotetramat-ketohydroxy was investigated in the same soils tested with the parent, which were once again sterilised using mercuric(II)chloride, and equilibration time was 24 h. For the adsorption phase, K_F values ranged from 0.52-2.21 mL/g, and the corresponding K_{FOC} values ranged from 41.0-99.1 mL/g. K_{OC} were close to the K_{FOC} with a range of 42.0-99.7 mL/g. The Freundlich exponent ranged from 0.92-0.93, indicating that adsorption is not dependent on concentration of the test substance. Following one round of desorption, the K_F values ranged from 0.67-2.84 mL/g, and the corresponding K_{FOC} values ranged from 51.4-170 mL/g. The 1.3-1.7× higher desorption coefficient values indicates this metabolite binds more weakly than the parent once adsorbed to the soil. Based on these values, spirotetramat-ketohydroxy is classified as highly mobile according to the classification scheme of McCall *et al.* (1980).

No significant breakdown of spirotetramat-MA-amide was observed in soil equilibrium experiments using the same soils and an equilibration time of 24 h. For the adsorption phase, K_F values ranged from 0.06-0.18 mL/g, and the corresponding K_{FOC} values ranged from 4.4-25.5 mL/g. K_{OC} were close to the K_{FOC} with a range of 4.2-25.6 mL/g. The Freundlich exponent arithmetic mean of 0.95 indicated that adsorption is not dependent on concentration of the test substance. Following one round of desorption, the K_F values ranged from 0.13-0.37 mL/g, and the corresponding K_{FOC} values ranged from 7.8-52.6 mL/g. The 1.6-2.3× higher desorption coefficient values indicates this metabolite binds more weakly than the parent once

adsorbed to the soil. Based on these values, spirotetramat-ketohydroxy is classified as highly mobile according to the classification scheme of McCall *et al.* (1980).

Owing to the extreme instability of spirotetramat-enol once in contact with soil, no reliable adsorption value could be determined for this metabolite in a standard batch equilibrium experiment according to guideline OECD 107. In an additional study to investigate time-dependent sorption, the adsorption and binding of this metabolite rapidly increased with aging time in soil, while the mobile fraction is degraded within a few hours (mainly to spirotetramat-ketohydroxy), indicating its absence from the soil pore water within a very short period of time. A column leaching study using spirotetramat-enol as parent was conducted on the same 4 soils used for the spirotetramat-enol degradation study, and found that by far the majority was sequestered (via chemisorption) within the topsoil layer, with only a small fraction of the metabolite having the potential to leach into deeper soil layers or leave the soil column (≤2.8% of AR in leachates). Only small amounts of the applied spirotetramat-enol were recovered in soil extracts and even smaller amounts in the leachate, indicating immediate and strong binding to the top soil, significant formation of NER, and the transformation to degradates. A K_{OC} range of 27–99 mL/g was calculated for the mobile phase, classifying spirotetramat-enol as highly mobile according to the classification scheme of McCall *et al.* (1980). However, this value represents the first phase of the distinct bi-phasic degradation, while the slowly degrading and strongly bound fraction (representing the second phase of the biphasic degradation) is considered more or less immobile. The K_{OC} values for spirotetramat-ketohydroxy and spirotetramat-MA-amide were comparable to results from the batch equilibrium experiments, indicating that the K_{OC} values obtained for spirotetramat-enol in the column leaching study are reliable.

According to the HPLC method, spirotetramat-enol dimer 1 and spirotetramat-enol dimer 2 show K_{OC} values of ~ 1624 and 3208 mL/g, respectively. Their respective classifications in accordance with McCall *et al.* (1980) are lowly and slightly mobile. However, neither spirotetramat-enol dimer 1 nor spirotetramat-enol dimer 2 is considered relevant for further risk assessment due to low formation in soil and water.

No adsorption/desorption constants are available for spirotetramat and metabolites in alkaline soils, however, no pH dependency on sorption was noted in the studies. Therefore, it is unlikely that adsorption/desorption under more alkaline conditions will significantly differ from values obtained in the tested range. This assumption is confirmed by modelling results from US field trials (topsoil pH of 6.3–8.1), where re-modelling with the (uncalibrated) parameter set used for spirotetramat and metabolites, based on K_{OC} values obtained from the tested pH range of 4.7–6.8, showed consistency between modelled and measured data in more alkaline soils.

Bioaccumulation

According to the OECD monograph, a bioaccumulation study was not submitted based on the log P_{OW} value of 2.51 for spirotetramat not triggering a requirement for this study. In addition, the log P_{OW} values at pH 7 for the environmentally metabolites in water/sediment studies, spirotetramat-enol and spirotetramat-ketohydroxy, are even lower at 0.3 and 1.3, respectively. The P_{OW} values for the major photolysis metabolites 4-methoxycyclohexanone and 4-methoxycyclohexylamino carboxylic acid were estimated using the programme ALOGPS 2.1 to range from -0.04-0.74 and -2.49-1.0, respectively. The lack of testing has been accepted by the primary and secondary reviewers and significant bioaccumulation of spirotetramat or its degradation products is unlikely to occur.

Foliage and arthropod residues

A study reported the results of multiple field trials investigating residues in wheat and soybean forage following successive applications to plots at 176 g ac/ha with the OD150

formulation, with application intervals of 19-21 days. The wheat trials included mowed and unmowed plots to represent short and tall grass, respectively. Maximum residues following the second application ranged from 10.28 ppm in soybean forage to 21.65 ppm in tall wheat grass. However, mean residues were highest on short wheat grass at 14.35 ppm. Total spirotetramat residues dissipated with DT50 values of ~2 days for short and tall wheat grass and ~4.5 days in soybean forage.

Another study investigated spirotetramat and metabolite residues in ground and foliage dwelling arthropods within citrus orchards. Following applications of 99.6 or 121.3 g ac/ha with a 1 metre canopy height (equivalent to 270 g ac/ha), maximum residues of the parent, parent + enol and total measured residues were 0.32, 0.60 and 0.62 ppm, respectively, for ground dwelling arthropods, and 4.0, 6.0 and 6.2 ppm, respectively, for foliage dwelling arthropods. The respective DT50 values for the latter were 2.8, 4.7 and 5.1 days.

ENVIRONMENTAL EFFECTS

Avian toxicity

There were 6 toxicity studies conducted with birds – 1 acute oral test and 2 acute dietary studies using spirotetramat, and 3 reproduction studies also with the active substance.

No significant compound related effects of mortality were observed in bobwhite quails orally exposed to spirotetramat, with an acute 14 day LD50 >2000 mg ac/kg body weight. However, 2 mortalities were observed following reduced activity, fluffed feathers, ptosis and apathy. Sublethal effects included reduced body weight over the first 7 days at the highest test concentration (followed by recovery), and reduced food consumption from days 1-3 at all treatment levels (500-2000 mg ac/kg body weight). Given the lack of data presentation in the monograph, it is unclear if these effects are dose-dependent. Although no effects on mortality were observed in quails and mallards following dietary exposure to spirotetramat, with 5 day LC50 values >4998 and >6050 mg ac/kg food, respectively, body weight and feed consumption were significantly affected in a dose-responsive manner, resulting in NOEC values of 1218 and <344 mg ac/kg food, respectively. Recovery was observed during the 3 day recovery period. Based on the results of these studies, spirotetramat would be classified as, at worst, slightly toxic to birds.

In a reproduction test with bobwhite quails, there was a 14% reduction in female weight gain and significant effects were also observed in some egg and hatching parameters, although the effects on reproduction (<6% compared to the control) were not considered biologically significant. The adult and reproduction NOEC values were 264 and 802 mg ac/kg feed, respectively. Mallard ducks were more sensitive, with 79% of surviving adults at the highest test concentration (869 mg ac/kg food) experiencing severe peeling and cracking of the foot webbing, resulting in immobility and emaciation as they could not eat or drink. As a result the birds were sacrificed at week 12, before reproduction parameters could be measured. The symptom was apparently dose-related, and was observed after 21 weeks in 54 and 27% of adults at the 269 and 89 mg ac/kg food groups, respectively. Adult weight gain was significantly affected, at ≥269 mg ac/kg food, however, it is unclear to what extent the foot effects contributed to the significance of this endpoint. Statistically significant effects were observed for most reproductive parameters at ≥269 mg ac/kg food. Based on these effects, the adult and reproduction NOEC values were <89 and 89 mg ac/kg food respectively. In a repeat study exposing mallard ducks to slightly lower dietary concentrations of spirotetramat, birds at the highest test concentration of 869 mg ac/kg food exhibited clinical signs of toxicity, including loss of coordination, lower limb weakness and cracked and bleeding foot lesions by week 3, and were euthanased by week 5. Foot lesions were evident in birds in the ≥80 mg ac/kg food group. Based on these effects, and effects on adult food consumption, offspring body weights, hatchability and egg production, the adult and reproduction NOEC value is 28.8 mg ac/kg food.

Two further studies were conducted to examine the cause of the foot effects displayed in ducks in the reproduction studies. In the first, ducks exposed to spirotetramat in their diet (at 720 mg ac/kg food) but with excrement periodically removed (no dermal exposure) displayed moderate to extreme dermal cracking, resulting in a reluctance to feed and emaciation. By contrast, dermal exposure to treated excrement resulted in less severe and more transient symptoms. In a second study, conducted in natural outdoor conditions, ducks exposed to a dietary concentration of spirotetramat at 200 mg ac/kg food and dermally exposed to oversprayed turf (applications of 158, 86.8 and 140 g ac/ha 14 days apart) displayed foot abnormalities (minor to severe cracking on the underside of the digits) by week 2 following treatment, along with limping, a reluctance to walk, sitting immediately after landing, stumbling while walking and a preference for flying over walking. The foot conditions were evident in up to 64% of birds and the number of severe cases increased until week 10. Significant recovery in foot condition was observed during the recovery period.

Fish toxicity

There were 7 acute toxicity studies conducted with fish – 3 with the active constituent, spirotetramat, 2 metabolite studies, and 1 with the OD150 formulation.

In a 96 hour semi-static test with rainbow trout (*Oncorhynchus mykiss*) exposed to spirotetramat, dose and time responsive mortality resulted in a 96 hour LC50 of 2.54 mg ac/L. Sublethal symptoms, including loss of equilibrium, laboured respiration, vertical position, and staying at the surface or bottom of the aquarium, were observed at concentrations ≥1.5 mg ac/L. Dose and time responsive mortality effects were also observed in the common carp (*Cyprinus carpio*), bluegill sunfish (*Lepomis macrochirus*), and the sheepshead minnow (*Cyprinodon variegatus*), with 96 hour LC50 values set at 2.59, 2.2 and 1.96 mg ac/L, respectively. Sublethal effects, observed at 1.71, 1 and 0.52 mg ac/L, respectively, included laboured respiration, dark colouration, laying on sides or back, hyperactivity, inactivity and convulsions in addition to those observed in rainbow trout. These sublethal effects were transient in the bluegill sunfish. Based on the results of these studies, spirotetramat would be classified as moderately acutely toxic to fish.

When rainbow trout were exposed to the metabolite spirotetramat-enol in a 96 hour static limit test, no compound related effects (survival or sublethal) were observed, and the 96 hour LC50 was set at >100 mg metabolite/L. Likewise, no mortalities were observed in zebra fish (*Danio rerio*) exposed to another metabolite, 4-methoxycyclohexanone, resulting in a 96 hour LC50 >100 mg metabolite/L. However, transient abnormalities in swimming were observed in 50% of fish. Based on the results of these studies, the spirotetramat metabolites spiroteramat-enol and 4-methoxycyclohexanone would be classified as practically non-toxic to fish.

Rainbow trout were more sensitive to the OD150 formulation of spirotetramat in a static test, with dose and time dependent mortalities resulting in a 96 hour LC50 value of 1.41 mg ac/L. Sublethal symptoms similar to those exhibited by fish exposed to spirotetramat (technical) were observed at ≥0.78 mg ac/L. Based on the result of this study, spirotetramat as the OD150 formulation, would be classified as moderately toxic to fish.

The chronic toxicity of spirotetramat to the early life stages of the fathead minnow was studied under flow-through conditions over 33 days (28 days post hatch). No treatment related effects on hatchability and growth parameters were observed. However, based on a reduction in overall fry survival, the 33 day NOEC was set at 0.534 mg ac/L and spirotetramat is classified as slightly chronically toxic to the fathead minnow, based on DEWHA classifications.

Aquatic invertebrate toxicity

There were 13 toxicity studies conducted with aquatic invertebrates – 6 with spirotetramat, 6 with 4 spirotetramat metabolites, and 1 with the OD150 formulation.

In a 48 hour static test with the waterflea (*Daphnia magna*) exposed to spirotetramat, dose-responsive effects on immobility (maximum 23%) were observed, resulting in an EC50 >42.7 mg ac/L and a NOEC value of 20.3 mg ac/L. Given the apparent dose response effect at the 2 highest test concentrations, and a mean measured concentration as low as 22% of the nominal concentration, 50% mortality could be expected at the maximum nominal concentration (100 mg ac/L). A clear dose-response effect on midges (*Chironomus riparius*) was observed in a 48 hour water-only study following exposure to spirotramat, resulting in a 48 hour LC50 value of 1.3 mg ac/L. However, the secondary reviewer noted that the test duration should be 96 hours, in addition to other deviations from USEPA guidelines, which may have overestimated the LC50 value. Dose dependent mortality and shell growth inhibition were observed in saltwater mysids (*Americamysis bahia*) and eastern oysters (*Crassostrea virginica*) exposed to spirotetramat under flowthrough conditions over 96 hours, resulting in LC50 and EC50 values of 5.5 and 0.83 mg ac/L, respectively. Sublethal effects including erratic swimming and laying at the bottom of the vessel were observed at ≥2.6 mg ac/L in the mysids. Based on the results of these studies, spirotetramat would be classified as slightly to highly toxic to aquatic invertebrates.

Waterfleas were not acutely sensitive to the metabolites spirotetramet-enol and 4-methoxycyclohexanone in static limit tests, resulting in 48 hour EC50 values >100 mg metabolite/L and no sublethal effects. A dose dependent effect on mortality (maximum 40%) was observed in midges exposed to the spirotetramat-enol under static (water-only) conditions, with a 48 hour LC50 value of 74.9 mg metabolite/L (extrapolated using Probit analysis). Under the same test conditions, low mortalities were observed in midges (maximum 27.5% mortality rate at the highest test concentration) exposed to spirotetramat-ketohydroxy, and none following exposure to 4-methoxycyclohexanone and spirotetramat-cis-methoxy-cyclohexylamino carboxylic acid, setting 48 hour LC50 values >100 mg metabolite/L. Based on the results of these studies, the metabolites would be classified as slightly to practically non-toxic to aquatic invertebrates.

In a result similar to the fish studies, midges were most sensitive to the formulated product. A dose response effect on mortality was observed in midges following exposure to the OD150 formulation of spirotetramat under static (water-only) conditions, and the LC50 value was set at 0.66 mg ac/L. Based on the results of these studies, spirotetramat would be classified as highly toxic to midges. Again, concerns were raised by the reviewer regarding deviations from USEPA guidelines.

The chronic toxicity of spirotetramat to daphnids was studied under semi-static conditions over 21 days. No treatment related effects on time to first brood were observed, however, reductions in offspring survival per parent and growth parameters were seen at the highest test concentration, resulting in a reproduction and growth NOEC value of 4.41 mg ac/L. The most sensitive endpoint was parent mortality, setting a 21 day NOEC value of 1.84 mg ac/L. In a static, water-spiked study over 28 days, emergence rates of midges were significantly reduced in a dose responsive manner, resulting in a 28 day NOEC value of 0.1 mg ac/L. Based on these results, spirotetramat is classified as very slightly to moderately chronically toxic to aquatic invertebrates.

Algal toxicity

There were 9 studies with algae and duckweed using the active constituent, 2 metabolites and the 150 OD formulation.

A dose responsive effect on biomass and growth inhibition was observed in green algae (*Pseudokirchneriella subcapitata*) following 72 hours of exposure (under static conditions) to spirotetramat, with EbC50 and ErC50 values of 6.58 and 8.15 mg ac/L, respectively, and a NOEC value of 1.46 mg ac/L. A similar pattern of inhibition was observed in the freshwater diatom (*Navicula pelliculosa*) following 96 hours of exposure, resulting in EC50 values of 4.05 and 15.0 mg ac/L for biomass and growth rate inhibition, respectively, and respective NOEC values of 0.19 and 1.0 mg ac/L. The blue-green alga (*Anabaena flos-aqua*) was less sensitive to the active constituent, with significant biomass inhibition at 5.68 mg ac/L but no significant inhibition to growth rate. The EC50 values were set at 15.2 and >15.1 mg ac/L for biomass and growth rate, respectively. With EC50 values of 0.36 (biomass) and 0.98 (growth rate) mg ac/L, the saltwater diatom (*Skeletonema costatum*) displayed the greatest sensitivity to the active constituent. In a 7 day study with aquatic plants, dose responsive inhibition was observed in duckweed (*Lemna gibba*), with a NOEC of 4.54 mg ac/L and EC50 values for biomass and growth rate of 4.62 and 6.21 mg ac/L, respectively. Based on the results of these studies, spirotetramat would be classified as slightly to highly toxic to algae and aquatic plants.

The green alga was not sensitive to the metabolites spirotetramat-enol and 4-methoxycyclohexanone, with EC50 values for biomass and growth rate >100 mg metabolite/L. Significant biomass and growth rate inhibition only occurred following exposure to the highest rate of the former, resulting in a NOEC value of 31 mg metabolite/L. Higher toxicity to the enol was observed in duckweed, where the EC50 values for biomass and growth rate were set at 5.4 and 19.3 mg ac/L, respectively. Based on the results of these studies, these metabolites would be classified as practically non-toxic to moderately toxic to algae and aquatic plants.

The spirotetramat OD150 formulation had a dose responsive effect similar to the technical active on biomass and growth inhibition in the green alga following 72 hours of exposure. The EC50 values for biomass and growth were 6.56 and >8.2 mg ac/L, with a NOEC of 2.02 mg ac/L. Based on the result of this study, the OD150 formulation is, at worst, moderately toxic to algae.

Terrestrial Invertebrate toxicity

There were 14 studies with terrestrial invertebrate species using the active constituent, 3 metabolites and the 150 OD and 240 SC formulations.

Mortalities in oral and contact toxicity studies with the honey bee (*Apis mellifera*) were 4 and 2%, respectively, giving respective 48 hour LD50 values of >107.3 and >100 µg ac/bee. No sublethal effects were observed. Exposure of bees to the OD 150 formulation resulted in clearly dose responsive mortalities, and 48 hour oral and contact LD50 values of 91.7 and 162 µg ac/bee. Based on these results, spirotetramat is slightly toxic to adult honeybees.

As spirotetramat has insect growth-regulating properties, a 21 day study with the OD 100 formulation was conducted under field conditions, with honeybees fed the test substance at a concentration of 0.0144% ac (144 mg ac/L in a sugar solution). While no significant effects on flight activity and behaviour of the bees around the hives were observed, adult and pupae mortality was more than double than that seen in the controls. This result was not seen as biologically relevant. However, 2 of the 3 hives showed a massively disrupted brood development 4 days after the start of feeding, which was not able to be compensated. In an identical test with the SC 240 formulation at the same feeding rate, similar results were observed with the exception that massive brood disruption occurred in all 3 hives during the first 5-15 days after feeding. However, a tendency to recover was apparent by day 21.

Application of the OD 150 formulation at a rate of 4×72 g ac/ha to *Phacelia tanacetifolia*, twice before flowering and twice after flowering (and during bee foraging), and in a separate

field at 2×96 g ac/ha after flowering, all at ~7 day intervals, resulted in no significant effects on adult and pupal mortality, flight intensity (supported by pollen in the combs of the colonies), condition of the colonies (as measured by colony strength and brood nest size), brood development or behaviour around the hives. A lack of eggs and/or larvae on the last 2 assessment dates in one of the 4×72 g ac/ha treatment colonies was attributed to a lack of space for the colony to grow, or from removal of the old queen.

In a tunnel test with the OD 100 formulation applied to spring rape at a rate of 3×72 g ac/ha prior to flowering followed by 2×96 g ac/ha after set up of the colonies, and in a separate field at 96 g ac/ha 3 days after set up of the colonies, no significant effects in adult and pupal mortality, flight intensity, condition of the colonies, and behaviour around hives was observed. Although retarded brood development was observed in certain treatment group colonies, this was also observed to some degree on control colonies, and all treatment and control colonies were in good condition during the 29 day observation period. Therefore, effects in the treatment colonies could not be clearly ascribed to the application of the test item. Concerns were raised by a secondary reviewer regarding the lack of statistics, although the much higher number of dead pupae post-feeding of the toxic standard compared to the control (as expected with an insect growth regulator) and spirotetramat treatment groups is evidence of massive disturbance brood development. Overall, spirotetramat appears to have low toxic effects to foraging bees, however, potential effects on brood development are apparent. Recovery is likely following dissipation of spirotetramat exposure with use of the proposed product (SC 240 formulation).

In 2 acute contact laboratory studies, the parasitoid wasp (*Aphidius rhopalosiphi*) and predatory mite (*Typhlodromus pyri*) were exposed to dried residues of the OD 150 formulation on glass plates for 48 hours and 7 days, respectively. Clear dose responsive mortality increases were observed in both tests, with wasps less sensitive (48 hour LR50 = 114.7 g ac/ha) than mites (7 day LR50 = 0.333 g ac/ha). Extension of these tests to freshly dried residues on barley leaves raised the 48 hour LD50 value for wasps to >288 g ac/ha, with no reduction in reproductive success (NOEC = 288 g ac/ha) following 11 days exposure to untreated oat plants infested with *Rhopalosiphum padi*. Again, greater sensitivity was observed in mites following exposure to fresh dried residues on *Phaseolus vulgaris*, with dose dependent mortality, a 7 day LR50 value of 1.59 g ac/ha and a significant reduction in reproduction at all rates with surviving mites (NOEC <0.15 g ac/ha). Based on this result, predatory mites were exposed in the laboratory over 7 days to aged residues (for up to 56 days under semi-field conditions with rain protection) on apple leaves which had been treated with 4×72 g ac/ha of the OD 150 formulation at 7 day intervals. Corrected mortalities ranged from 90.5-100% over the first 28 days, with a subsequent time responsive reduction in mortality rate over the next 28 days to ~50% by day 49 and ~11% by day 56. No adverse effects on reproduction were observed, with a ~14% increase compared to the control.

Further extended laboratory studies were conducted by exposing green lacewings (*Chrysoperla carnea*) and ladybird beetles (*Coccinella septempunctata*) to fresh dried residues of the OD 150 formulation of spirotetramat on bean leaves and in their food, *Sitotroga* eggs. Based on low effects on mortality and reproduction, 24 d (green lacewing; unspecified time for mites) LR50 values of 288 g ac/ha and NOEC values of 288 g ac/ha were set for both species.

In a study investigating the effects on mite fauna in grape vines, the OD 150 formulation of spirotetramat was applied ranging from twice (14 days apart) at rates of 96 g ac/ha (and lower to represent drift events), to 4 times (7 days apart) at 4.8 g ac/ha. Population changes relative to the water control were taken shortly before each application, 1 week after the first application and ~1, 4 and 8 or 9 weeks after the last application, from analysis of the washings of 3 leaves from each of the 8 innermost vines of a plot. The most abundant species was the predatory mite, and although this was shown to be very sensitive in the extended laboratory tests, the only statistically significant difference compared to the control was observed in the

lowest drift treatment rate 5 days after the first treatment, but not at subsequent sampling points. In addition, no Abbott corrected mortalities exceeded 50% (highest 43%). The study was considered valid since application of the toxic reference resulted in significant reductions (43-96%) of mites at all sampling times.

Earthworms (*Eisenia fetida*) were not acutely sensitive to spiroteramat or to the metabolite spirotetramat-ketohydroxy, with a 14 day LC50 value >1000 mg ac/kg dry soil, and no effects on mortality and body weight, resulting in a 14 day NOEC value of 1000 mg ac/kg dry soil. No mortalities were observed following exposure to the metabolite 4-methoxycyclohexanone (14 day LC50 >1000 mg metabolite/kg dry soil). However, a dose responsive reduction in body weight was apparent, resulting in a NOEC value for body weight of 125 mg metabolite/kg dry soil. In a chronic toxicity test exposing earthworms to spirotetramat-enol over 56 days, mortality and body weight were not affected, giving LC50 and NOEC values of >1000 and 1000 mg metabolite/kg dry soil. However, reproduction was significantly reduced, with a reproduction EC50 value of 1269 mg metabolite/kg dry soil, but a NOEC value of 32 mg/kg dry soil.

In a 21 day reproduction study with the gamasid mite (*Hypoaspis aculeifer*), mortality was significantly reduced at the highest test concentration, setting the LC50 value at >1000 mg metabolite/kg dry soil, and the NOEC value at 316 mg metabolite/kg dry soil. No adverse effects on reproduction were observed.

Microbial toxicity

There were 3 studies investigating the effects on soil microflora from exposure to the active constituent.

Following addition of spirotetramat to soil at rates of 0.13 and 1.32 mg ac/kg dry soil (99 and 990 g ac/ha) in 2 separate tests investigating effects on nitrogen and carbon transformation, no reductions <25% compared to the control were observed after 28 days for either microbial process, although reductions above this trigger value occurred on days 7 and 14. Respiration in activated sewage sludge was not inhibited at concentrations up to 10,000 mg ac/L.

Terrestrial plant toxicity

There were 5 terrestrial plant studies presented for assessment; 2 seedling emergence studies and 3 vegetative vigour tests. In the first seedling emergence study, 6 crop species were treated at 288 g ac/ha with percent emergence and survival ranging from 95-100% after 14 days. No phytotoxicity or differences in growth stages compared to the control were observed. The maximum biomass reduction was 10% in corn, however, this was well below the 50% trigger for further testing. In a repeat study with 10 crops treated at 176 g ac/ha and conducted over 21 days, again there were no biologically significant effects on germination or growth of the emerged seedlings. Canola was the most sensitive species with 80% emergence and 84% seedling survival after 21 days. No inhibition effect >19% was observed in growth endpoints. Similar phytotoxicity symptoms were observed in both the treatment group and controls.

In the first vegetative vigour test (a non-GLP study) the leaves and above-ground portions of 6 crop plants were treated at 288 g ac/ha. While there were no adverse effects on survival (mostly 100% survival but 95% in cucumbers), visible signs of phytotoxicity such as chlorosis, necrosis, leaf deformation, bleaching and/or stunting were observed in all crops tested, and were particularly severe in canola, while symptoms in corn, cucumbers, sunflowers and oats were moderate to severe. Biomass was statistically significantly reduced in all species tested, and the 50% inhibition trigger value was exceeded by canola, corn and oats. Again, canola was the most sensitive species, with an 83.3% inhibition in dry weight. Further testing on 10 species treated at 11-176 g ac/ha indicated complete survival of all plant species. Consistent phytotoxicity throughout the study period was observed in corn and ryegrass, with minor or random effects in canola, oats and onions. Growth parameters in

ryegrass were sensitive to spirotetramat at the highest test concentration, resulting in a NOEC of 88 g ac/ha and an EC25 value of 168 g ac/ha. Corn was the most sensitive species with >50% inhibition of plant length and dry weight resulting in a NOEC value of 44 g ac/ha and an EC25 value of 76 g ac/ha. In the final test, corn, oats and canola were exposed over 21 days to 26-288 g ac/ha. All plants survived, but similar dose responsive effects on fresh shoot weight were observed in all 3 species, with significant inhibitory effects at higher concentrations, but none >50%. Necrosis and chlorosis was apparent in corn only. The resultant NOEC value was 72 g ac/ha, based in growth inhibition in canola, and the overall EC50 value was >288 g ac/ha.

ENVIRONMENTAL RISK ASSESSMENT

Spirotetramat is unlikely to cause adverse effects in aquatic species and terrestrial plant species following ground applications to brassica vegetables. Spray drift modelling established that buffers are not required for applications conducted in accordance with the proposed label. In addition, the risk to aquatic species from runoff is acceptable. Likewise, mammals and soil microorganisms are unlikely to be harmed. Avian species are not acutely sensitive to spirotetramat, but chronic exposure was shown to cause reproductive adverse effects and clinical symptoms of toxicity, including severe foot cracking and lesions. However, the effect concentrations were higher than the maximum predicted environmental concentration. In addition, chronic exposure is unlikely given the low persistence of spirotetramat on foliage, and birds are expected to quickly recover from these symptoms following dissipation of the active constituent. Spirotetramat has a range of effects on terrestrial invertebrates. Soil invertebrates such as earthworms and gamasid mites are unlikely to be harmed. Likewise, adverse effects on wasps, lacewings and ladybird beetles are not expected following applications to brassica vegetables at the maximum proposed rate. Honeybees are not sensitive to acute exposure or residues from direct overspray, but massive brood disruption has been observed in field feeding studies. However, complete recovery is expected following dissipation of spirotetramat, when using the SC 240 formulation. Significant adverse effects on predatory mites were observed in laboratory tests, but were less sensitive in field tests at less than the proposed maximum seasonal rate. Based on the extended laboratory tests, a potential risk may be expected to predatory mites populating a sprayed area for up to 7 weeks following application. This result indicates that the use of the active constituent may not be complementary with integrated pest management (IPM).

JUSTIFICATION FOR USE AND MODE OF ACTION

This application seeks the registration of *MOVENTO 240 SC INSECTICIDE (MOVENTO)*, which contain spirotetramat as its only active constituent. The proposed use is for application as a foliar spray for the control of silverleaf whitefly in various brassica vegetable crops (broccoli, broccolini, Brussels sprouts, cabbage and cauliflower).

Sprirotetramat is the first member of a new chemical class, the cyclic ketoenoles. It is a tetramic acid derivative with a novel mode of action that interferes with lipid biosynthesis. The active constituent is active against a wide spectrum of sucking insects, including aphids, scales (soft and armoured), mealybugs, whiteflies, psyllids and selected thrip species. Acceptable safety to in-crop non-target organisms has been demonstrated.

Proposed use pattern

MOVENTO will be applied to various brassica vegetable crops (broccoli, broccolini, Brussels sprouts, cabbage, and cauliflower) as a foliar spray with up to three sequential applications of the product at no less than 7-day intervals. The product application rate for *MOVENTO* is 300 to 400mL/ha for silverleaf whitefly (*Bemisia tabaci* Biotype B). The higher application rates are used during periods of high pest pressure, rapid crop growth, or when longer residual control is desired.

Use is proposed for all States and territories.

It is proposed that *MOVENTO* will be available in 1L, 2.5L, 5L, and 10L high-density polyethylene containers.

The following Withholding Period statements are recommended for the product:

Harvest (H)

Brassica vegetables: DO NOT harvest for 3 days after application.

DO NOT use on brassicas grown for forage or fodder.

EVALUATION OF EFFICACY AND CROP SAFETY

Four field trials in brassica crops (3 x cauliflower and 1 x broccoli) conducted in the Lockyer Valley in southeast Queensland were presented to demonstrate the efficacy of *MOVENTO* for control of silverleaf whitefly (*Bemisia tabaci* Biotype B). *MOVENTO* was tested at rates of 100 to 500 mL/ha with a range of spray adjuvants (Hasten®, Agral® and a Nufarm surfactant) and compared with the industry standards Applaud®, Admiral®, and Chess®. The trials were all randomized complete block designs with four to five replicates. The pest density of silverleaf whitefly was moderate to heavy. The water rate used in the trials varied from 315 to 440L/ha. *MOVENTO* was applied once in three trials and three times at 14-day intervals in the fourth trial.

The results were consistent and showed significant reduction in numbers of nymphal stages and eggs, with levels of reduction up to 100%. In one of the two trials, which assessed adult silverleaf whitefly numbers, *MOVENTO* showed significant reduction in adult numbers. The levels of efficacy were similar to, or better than the industry standards used (Applaud®, Admiral®, and Chess®). A rate response was shown in three of the trials with rates of 300 to 500mL/ha performing better than the lower rates. Three of the trials showed that single applications provide a significant effect from five to 36 days. There was no clear effect of using any one adjuvant. The use of Hasten® at 1% and 1L/ha provided similar efficacy. No

phytotoxicity was observed on brassica crops in any of the four efficacy trials, which were conducted at a range of below, at and above label rates. Based on the efficacy and crop safety results, it is accepted that, at the proposed rates of 300 to 400 mL/ha, MOVENTO would not pose unacceptable risks to applied crops and would be effective for controlling silverleaf whitefly in brassica crops.

Four laboratory experiments and one field trial were presented to demonstrate safety on non-target plants. The non-target plants consisted of tomato, cucumber, oilseed rape, soybean, sunflower, shattercane (type of sorghum), sugar beet, potato, corn, oats, wheat and onion. The product was applied at high rates equivalent to 400 to 900 mL/ha in the laboratory experiments, and 300 to 500mL/ha in the field trial. These experiments and field trial were designed as paired control.

Overall *MOVENTO* did not show significant effects on the germination, survival, phytotoxicity, and dry weight of the plants tested in the laboratory experiments. The field trial showed no observable phytotoxicity on tomato, sunflower, wheat, onion or potatoes. Based on the results, it is accepted that, at the proposed rates of 300 to 400 mL/ha, MOVENTO would not pose unacceptable risks to non-target plants.

Integrated Pest Management

Two field trials were provided to demonstrate safety to beneficial invertebrates. The field trials were completed on cotton crops and were randomized complete blocks with four replicates. At the rate of 300 to 900mL/ha, acceptable safety to beneficial invertebrates including spiders, predatory bugs, predatory beetles, and hymentoptera wasps was demonstrated. When negative impacts were detected, the level of impact was similar to or lower than industry standards endosulfan and Talstar®.

At rates of over 1000mL/ha *MOVENTO* did not have a significant negative effect on mortality or reproduction of the parasitic wasp, green lacewing, and the ladybird beetle. There was a low level of mortality observed on the predatory mite at 300 to 900mL/ha and to address this risk the applicant has amended the label to include a statement regarding the effect of *MOVENTO* on beneficial insects. Based on the general pattern of beneficial impact data, it is accepted that, at the proposed rates of 300 to 400mL/ha, *MOVENTO* would not pose unacceptable risk to beneficial invertebrates.

Conclusion

Sufficient statistically analysed data from suitably designed and scientifically conducted trials has been presented to substantiate the claims for use shown on the proposed labels. The data demonstrate that the product *MOVENTO* should be suitable for control of silverleaf whitefly in some brassica vegetable crops (broccoli, broccolini, Brussels sprouts, cabbage, and cauliflower), when used in accordance with the proposed label instructions and Good Agricultural Practice (GAP).

MAIN PANEL

POISON

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

Movento® 240 SC

INSECTICIDE

ACTIVE CONSTITUENT: 240 g/L SPIROTETRAMAT

GROUP	23	INSECTICIDE

For the control of silverleaf whitefly in certain Brassica vegetables as specified in the DIRECTIONS FOR USE table.

*** L**

IMPORTANT: READ THE ATTACHED BOOKLET BEFORE USE

(Label code)

* 1, 2.5, 5, 10 L

MOVENTO 240 SC INSECTICIDE

STORAGE AND DISPOSAL

Store in the closed, original container in a cool, well-ventilated area. Do not store for prolonged periods in direct sunlight.

1 litre container

Rinse containers before disposal. Add rinsings to spray tank. Do not dispose of undiluted chemicals on site. Dispose of at a local authority landfill. If no landfill is available, bury the containers below 500 mm in a disposal pit specially marked and set up for this purpose clear of waterways, desirable vegetation and tree roots. Empty containers and product should not be burnt. Do not re-use empty container for any other purpose.

2.5, 5, 10 litre containers

Triple or preferably pressure rinse containers before disposal. Add rinsings to spray tank. Do not dispose of undiluted chemicals on site. If recycling, replace cap and return clean containers to recycler or designated collection point.If not recycling, break, crush, or puncture and bury empty containers in a local authority landfill. If no landfill is available, bury the containers below 500 mm in a disposal pit specifically marked and set up for this purpose clear of waterways, desirable vegetation and tree roots. Empty containers and product should not be burnt. Do not re-use empty container for any other purpose.

SAFETY DIRECTIONS

May irritate the eyes. Repeated exposure may cause allergic disorders. Avoid contact with eyes and skin. When opening the container and preparing spray, wear cotton overalls buttoned to the neck and wrist (or equivalent clothing) and elbow length chemical resistant gloves. If product on skin immediately wash area with soap and water. If product in eyes wash it out immediately with water. 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 (telephone 131126).

MATERIAL SAFETY DATA SHEET

Additional information is listed in the Material Safety Data Sheet, which can be obtained from www.bayercropscience.com.au.

EXCLUSION OF LIABILITY

This product must be used strictly as directed, and in accordance with all instructions appearing on the label and in other reference material. So far as it is lawfully able to do so, Bayer CropScience Pty Ltd accepts no liability or responsibility for loss or damage arising from failure to follow such directions and instructions.

APVMA Approval No.:

IMPORTANT: READ THE ATTACHED BOOKLET BEFORE USE

REAR PANEL (cont.)

*

FOR 24 HOUR SPECIALIST ADVICE IN EMERGENCY ONLY PHONE **1800 033 111**	BARCODE

Bayer CropScience Pty Ltd
ABN 87 000 226 022
391-393 Tooronga Rd
East Hawthorn Vic. 3123

Phone: (03) 9248 6888
Fax: (03) 9248 6800
Website: www.bayercropscience.com.au
Technical Enquiries: 1800 804 479

(Label code)

Batch Number:
Date of Manufacture:

* drumMUSTER logo required for 2.5, 5, 10 L pack only

POISON

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

MOVENTO 240 SC INSECTICIDE

ACTIVE CONSTITUENT: 240 g/L SPIROTETRAMAT

For the control of silverleaf whitefly in certain Brassica vegetables as specified in the DIRECTIONS FOR USE table.

STORAGE AND DISPOSAL

Store in the closed, original container in a cool, well-ventilated area. Do not store for prolonged periods in direct sunlight.
The method of disposal of the container depends on the container type. Read the 'Storage and Disposal' instructions on the label that is attached to the container.

SAFETY DIRECTIONS

May irritate the eyes. Repeated exposure may cause allergic disorders. Avoid contact with eyes and skin. When opening the container and preparing spray, wear cotton overalls buttoned to the neck and wrist (or equivalent clothing) and elbow length chemical resistant gloves. If product on skin immediately wash area with soap and water. If product in eyes wash it out immediately with water. 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 (telephone 131126).

MATERIAL SAFETY DATA SHEET

Additional information is listed in the Material Safety Data Sheet, which can be obtained from www.bayercropscience.com.au.

EXCLUSION OF LIABILITY

This product must be used strictly as directed, and in accordance with all instructions appearing on the label and in other reference material. So far as it is lawfully able to do so, Bayer CropScience Pty Ltd accepts no liability or responsibility for loss or damage arising from failure to follow such directions and instructions.

APVMA Approval No.:

IMPORTANT: READ THIS BOOKLET BEFORE USE

Bayer CropScience

DIRECTIONS FOR USE
Restraints
DO NOT use on Brassicas grown for forage or fodder
DO NOT apply using aircraft

Spray Drift Restraints
DO NOT apply with smaller than **MEDIUM** spray droplets according to ASAE S572 definition for standard nozzles.
DO NOT apply when wind speed is less than 3 or more than 20 kilometres per hour at the application site.
DO NOT apply during surface temperature inversion conditions at the application site.

Mandatory No-Spray Zones
DO NOT apply if there are livestock, pasture or any land that is producing feed for livestock within **10 metres** downwind from the application area.

CROP	PEST	RATE	CRITICAL COMMENTS
Brassica vegetables (broccoli, broccolini, Brussels sprouts, cabbage, cauliflower)	Silverleaf whitefly (*Bemisia tabaci* Biotype B)	300 - 400 mL/ha plus adjuvant*	Monitor crops and commence applications once local thresholds are reached. Use the higher rate when periods of high pest pressure or rapid crop growth are evident or when longer residual control is desired. Continue to monitor crops and make subsequent applications as necessary. Do not re-apply within 7 days of a previous Movento spray. **Do not apply more than 3 applications per crop.** Ensure thorough coverage of the target crop – refer “Application” section in GENERAL INSTRUCTIONS. *** Always add a specified spray adjuvant – refer “Adjuvant” section in GENERAL INSTRUCTIONS.**

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

WITHHOLDING PERIOD
Brassicas: DO NOT HARVEST FOR 3 DAYS AFTER APPLICATION

Export of treated produce
Growers should note that MRLs or import tolerances do not exist in all markets for edible produce treated with Movento 240 SC. If you are growing edible produce for export, please check with Bayer CropScience Pty Ltd for the latest information on MRLs and import tolerances before using Movento 240 SC.

GENERAL INSTRUCTIONS

Insecticide Resistance Warning

GROUP	23	INSECTICIDE

For insecticide resistance management Movento 240 SC Insecticide is a Group 23 insecticide.
Some naturally occurring insect biotypes resistant to Movento 240 SC and other Group 23 insecticides may exist through normal genetic variability in any insect population. The resistant individuals can eventually dominate the insect population if Movento 240 SC or other Group 23 insecticides are used repeatedly. The effectiveness of Movento 240 SC on resistant individuals could be significantly reduced. Since occurrence of resistant individuals is difficult to detect prior to use, Bayer CropScience Pty Ltd accepts no liability for any losses that may result form the failure of Movento 240 SC to control resistant insects.
Movento 240 SC may be subject to specific resistance management strategies. For further information contact your local supplier, Bayer CropScience representative or local agricultural department agronomist.

Adjuvant

Apply Movento 240 SC with Hasten Spray Adjuvant** according to the manufacturer's label recommendation, i.e. generally apply Hasten at 0.5 to 1.0 L/ha. This can be achieved by adding Hasten at 200 mL/100 L of spray mixture, up to a maximum of 1.0 L/ha where application volumes exceed 500 L/ha. (** or other specified adjuvant – refer to Bayer CropScience for information).

Mixing

Shake the container well before using. Partially fill the spray tank with clean water and add the required volume of product to the water whilst agitating. Top up the tank with clean water to the required volume. Add the required amount of Hasten Spray Adjuvant. Movento 240 SC should be applied as soon after mixing as possible.

Application

Application should be by ground spray equipment only. Thorough coverage of the target area is essential. Apply in sufficient water, and using suitable application parameters (nozzles, pressure, boom height, speed, swath width, etc.) to ensure thorough and even coverage. Adjust water volumes according to the crop growth stage. Use only MEDIUM spray droplets according to ASAE S572 definition for standard nozzles.

Compatibility

For the latest information on the compatibility of Movento 240 SC with other products, contact your local Bayer CropScience Area Manager or your local reseller.

Integrated Pest Management

Movento may have an adverse effect on predatory mites where IPM is practised.

PRECAUTION

Re-entry period

Do not allow entry into treated areas until the spray has dried, unless wearing cotton overalls buttoned to the neck and wrist (or equivalent clothing) and chemical resistant gloves. Clothing must be laundered after each day's use.

PROTECTION OF WILDLIFE, FISH, CRUSTACEANS AND ENVIRONMENT
Toxic to aquatic organisms. DO NOT contaminate streams, rivers or waterways with the chemical or used containers.

PROTECTION OF CROPS, NATIVE AND OTHER NON-TARGET PLANTS
Application of Movento 240 SC to crops/plants other than those specified on this label may cause symptoms of phytotoxicity.
DO NOT apply under weather conditions or from spraying equipment that may cause spray to drift onto nearby crops/plants, cropping lands or pastures.

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GLOSSARY

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

REFERENCES

Australian Pesticides and Veterinary Medicines Authority 1996, *Ag Manual: The Requirements Manual for Agricultural Chemicals*, APVMA, Canberra. (See footnote below)

Australian Pesticides and Veterinary Medicines Authority 1997, *Ag Requirements Series: Guidelines for Registering Agricultural Chemicals*, APVMA, Canberra. (See footnote below)

Australian Pesticides and Veterinary Medicines Authority 1996, *MRL Standard: Maximum Residue Limits in Food and Animal Feedstuffs*, APVMA, Canberra. (See footnote below)

Australian Pesticides and Veterinary Medicines Authority 2001, *Ag Labelling Code—Code of Practice for Labelling Agricultural Chemical Products*, APVMA, Canberra. (See footnote below)

Australian Safety and Compensation Council, 2007, 'Hazardous Substances Information System, http://hsis.ascc.gov.au/Default.aspx

AUSVEG 2007a, 'Vegetable Spotlight Broccoli', 01-01 2007, http://www.ausveg.com.au/assets/contentitems/public/1553/VegetableSpotlight-Broccoli.pdf.

AUSVEG 2007a, 'Vegetable Spotlight Cauliflower', 01-01 2007, http://www.ausveg.com.au/assets/contentitems/public/1555/VegetableSpotlight-Cauliflower.pdf.

Burt J. 2001, 'Growing Brussels sprouts in Western Australia. Farmnote 34/2001. Department of Agriculture, Western Australia', 2001, http://www.agric.wa.gov.au/pls/portal30/docs/FOLDER/IKMP/HORT/VEG/CP/BROCCOLI/F03401.PDF

Chen, X., & Anderson, J.J.B., 2002, 'Isoflavones and bone: animal and human evidence of efficacy', *Journal of Musculoskel Neuron Interat,* vol. 2, no. 4, pp. 352-359.

Davis, B.N.K. & Williams C.T. 1990, 'Buffer zone widths for honeybees from ground and aerial spraying of insecticides', *Environmental Pollution,* 63:247-259

Dimsey, R. 1995, 'Agriculture Notes Growing Cauliflowers', AG0421, June 1995, State of Victoria, Department of Primary Industries, http://www.dpi.vic.gov.au/dpi/nreninf.nsf/childdocs/-71e8091f577d52d24a2568b30004f3b2-f35b1cac4054922bca256bc8000291d4-14638b6e6ad048a94a256dea00273ddf-e41cce62e4a78646ca256bcf000bbfb7?open.

Dimsey, R. 1997, 'Agriculture Notes Cabbage Growing', AG0499, August 1997, State of Victoria, Department of Primary Industries, http://www.dpi.vic.gov.au/dpi/nreninf.nsf/9e58661e880ba9e44a256c640023eb2e/d78472c6821c5ea8ca256f0e00032f7c/$FILE/AG0499.pdf.

Dimsey, R. 1998, 'Agriculture Notes Growing Broccoli', AG0074, April 1998, State of Victoria, Department of Primary Industries, http://www.dpi.vic.gov.au/DPI/nreninf.nsf/9e58661e880ba9e44a256c640023eb2e/37061ec954ac14f5ca256f150082c944/$FILE/AG0074.pdf.

Doerge, D.R., & Sheehan, D.M., 2002, 'Goitrogenic and estrogenic activity of soy isoflavones', *Environmental Health Perspectives* 110: Supplement 3, pp. 349-353.

Erdman, J.W., et al., 2005, 'Flavonoids and Heart Health', Proceedings of the ILSI North American Flavonoids Workshops, May 31-June 1, 2005, Washington, DC., *The Journal of Nutrition,* Supplement 718S-737S.

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.

Fletcher, J.S. et al., 1994, "Literature review and evaluation of the EPA food chain (Kenaga) nomogram, an instrument for estimating pesticide residues in plants, *Environmental Toxicology and Chemistry,* vol. 13, no. 9, pp. 1383-1391.

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.

Heemers, H., et al., 2003, 'Androgens stimulate coordinated lipogenic gene expression in normal target tissues in vivo', *Molecular Cell Endocrinology,* vol. 205, no. 1-2, pp. 21-31.

Kovacs, W.J., & Olsen., N.J., 1987, 'Androgen receptors in human thymocytes', *The Journal of Immunology,* vol. 139, no. 2, pp. 490-493.

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

McCall, P.J., Swann, R.L., Laskowski, D.A., Unger, S.M., Vrona, S.A., & Dishburger, H.J., 1980, 'Estimation of Chemical Mobility in Soil from Liquid Chromatographic Retention Times, *Bulletin of Environmental Contamination Toxicology,* vol. 24, pp. 190-195

Mensink, B.J.W.G., Montforts, M., Wijkhuizen-Maslankiewicz, L., Tibosch, H, & Linders, J.B.H.J., 1995, Manual for summarising and evaluating the environmental aspects of pesticides, Report No. 679101022, National Institute of Public Health and the Environment, The Netherlands.

Murison, J., & Napier, T., 2006, Primefact 90, July 2006m 'Cabbage growing', New South Wales Department of Primary Industries, http://www.dpi.nsw.gov.au/__data/assets/pdf_file/80168/Cabbage-growing---Primefact-90-final.pdf.

National Occupational Health and Safety Commission, 2004, 'Approved Criteria for Classifying Hazardous Substances', AusInfo, Canberra, NOHSC:1008(2004).

OECD, 2007a, 'Spirotetramat: final monograph', Annex B, B.9 Fate and Behaviour in the Environment.

OECD, 2007a, 'Spirotetramat: final monograph', Annex B, B.9 Ecotoxicology

Pass, D., Freeth, G., 1993, 'The Rat', ANZCCART Fact Sheet. *ANZCCART News*, vol. 6, no. 4, Summer 1998 Insert, http://www.adelaide.edu.au/ANZCCART/publications/Rat_15.pdf.

Pfleeger, T.G., Fong, A., Hayes, R., Ratsch, R., & Wickliff, F., 1996 'Field Evaluation of the EPA (Kenaga) Nomogram, a Method for Estimation Wildlife Exposure to Pesticide Residues on Plants', *Environmental Toxicology and Chemistry,* vol. 15, no. 4, pp. 535-543.

Philip, B., 1995, "Brussels Sprouts, In Horticulture Australia', Coombs, B., editor, 1995, Morescope Publishing Pty Ltd, Victoria, Australia.

Regulatory note – Spirodiclofen, 2006, REG2006-06, Pest Management Regulatory Agency, Health Canada.

Savino, W., & Dardenne, M., 2000, 'Neuroendocrine control of thymus physiology', *Endocrine Reviews,* vol. 21, no. 4, pp. 412-443.

Spiromesifen; Pesticide Tolerance, 2005, USEPA – Federal Register: April 27, 2005, vol. 70, no. 80, pp. 21631-21641, http://www.epa.gov/EPA-PEST/2005/April/Day-27/p8120.htm

Tan, D., & Deuter, P., 2004, 'Broccoli development, yield and quality: Importance of temperature', Queensland Government Department of Primary Industries and Fisheries.

Urban, D.J., & Cook, N.J., 1986, Hazard Evaluation Division, 'Standard Evaluation Procedures: Ecologucal Risk Assessment', US Environment Protection Agency, Office of Pesticide Program, Washington, DC, EPA 540/9-85-001.

Footnote:
Updated versions of these documents are available on the APVMA website http://www.apvma.gov.au.

APVMA PUBLICATIONS ORDER FORM

To receive a copy of the full technical report for the evaluation of spirotetramat in the product Movento 240 SC Insecticide, please fill in this form and send it, along with payment of $30 to:

Colin McCormack
Pesticides Contact Officer
Australian Pesticides and Veterinary Medicines Authority
PO Box E240
Kingston ACT 2604

Alternatively, fax this form, along with your credit card details, to:
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