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Proposed Registration Decision

Spirotetramat

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Overview

Proposed Registration Decision for Spirotetramat

Health Canada's Pest Management Regulatory Agency (PMRA), under the authority of the *Pest Control Products Act* and Regulations, is proposing full registration for the sale and use of Spirotetramat Technical Insecticide, Movento 150 OD Insecticide and Movento 240 SC Insecticide containing the technical grade active ingredient spirotetramat to control a variety of insect pests on field vegetable crops, tree fruits, hops, grapes (excluding table grapes) and small fruit vine crops.

An evaluation of available scientific information found that, under the approved conditions of use, the products have value and do not present an unacceptable risk to human health or the environment.

This Overview describes the key points of the evaluation, while the Science Evaluation provides detailed technical information on the human health, environmental and value assessments of Spirotetramat Technical Insecticide, Movento 150 OD Insecticide and Movento 240 SC Insecticide.

What Does Health Canada Consider When Making a Registration Decision?

The key objective of the *Pest Control Products Act* is to prevent unacceptable risks to people and the environment from the use of pest control products. Health or environmental risk is considered acceptable[1] if there is reasonable certainty that no harm to human health, future generations or the environment will result from use or exposure to the product under its proposed conditions of registration. The Act also requires that products have value[2] when used according to label directions. Conditions of registration may include special precautionary measures on the product label to further reduce risk.

To reach its decisions, the PMRA applies modern, rigorous risk-assessment methods and policies. These methods consider the unique characteristics of sensitive subpopulations in humans (e.g. children) as well as organisms in the environment (e.g. those most sensitive to environmental contaminants). These methods and policies also consider the nature of the effects observed and the uncertainties present when predicting the impact of pesticides. For more information on how the PMRA regulates pesticides, the assessment process and risk reduction programs, please visit the PMRA's website at http://www.pmra-arla.gc.ca.

[1] "Acceptable risks" as defined by subsection 2(2) of the *Pest Control Products Act.*

[2] "Value" as defined by subsection 2(1) of the *Pest Control Products Act* "...the product's actual or potential contribution to pest management, taking into account its conditions or proposed conditions of registration, and includes the product's (a) efficacy; (b) effect on host organisms in connection with which it is intended to be used; and (c) health, safety and environmental benefits and social and economic impact."

Before making a final registration decision on spirotetramat, the PMRA will consider all comments received from the public in response to this consultation document.[3] The PMRA will then publish a Registration Decision document[4] on spirotetramat, which will include the decision, the reasons for it, a summary of comments received on the proposed final registration decision and the PMRA's response to these comments.

For more details on the information presented in this Overview, please refer to the Science Evaluation of this consultation document.

What Is Spirotetramat?

Spirotetramat is an insecticide applied directly onto the leaves of plants for the control of sucking pests such as mites and aphids. It is applied to a variety of crops, including fruits and vegetables. Spirotetramat inhibits lipid biosynthesis in target insects and is most effective against immature insect life stages.

Health Considerations

Can Approved Uses of Spirotetramat Affect Human Health?

Spirotetramat is unlikely to affect your health when Movento 150 OD Insecticide and Movento 240 SC Insecticide are used according to label directions.

Potential exposure to spirotetramat may occur through the diet (food and water) or when handling and applying the product. When assessing health risks, two key factors are considered: the levels where no health effects occur in animal testing and the levels to which people may be exposed. The dose levels used to assess risks are established to protect the most sensitive human population (e.g. children and nursing mothers). Only uses for which the exposure is well below levels that cause no effects in animal testing are considered acceptable for registration.

Toxicology studies in laboratory animals describe potential health effects from varying levels of exposure to a chemical and identify the dose where no effects are observed. The health effects noted in animals occur at doses more than 100 times higher (and often much higher) than levels to which humans are normally exposed when spirotetramat products are used according to label directions.

Spirotetramat Technical Insecticide was moderately irritating to the eyes and was a dermal sensitizer in animals. Consequently, the statements "Warning—Eye Irritant" and "Potential Skin Sensitizer" are required on the label. End-use product Movento 150 OD Insecticide was considered to be of slight acute systemic toxicity, was severely irritating to the eyes and was a dermal sensitizer in animals. For these reasons, the statements "Danger—Eye Irritant", "Potential Skin Sensitizer" and "Poison" (accompanied by the appropriate symbol) are required on the label. End-use product Movento 240 SC

[3] "Consultation statement" as required by subsection 28(2) of the *Pest Control Products Act*.

[4] "Decision statement" as required by subsection 28(5) of the *Pest Control Products Act.*

Insecticide was a dermal sensitizer in animals, thus requiring the label statement "Potential Skin Sensitizer".

Spirotetramat did not cause cancer in animals and was not genotoxic. Spirotetramat did exhibit neurotoxic effects following acute exposure in the rat and repeat dosing in the dog. The male reproductive system (testis and sperm) was also targeted in the rat at high doses. The first signs of toxicity in animals given daily doses of spirotetramat over longer periods of time were decreases in thyroxine (T4), decreased thymus size with increased incidence of thymus involution and dilatation of the cerebral brain ventricles in dogs. The risk assessment protects against these effects by ensuring that the level of human exposure is well below the lowest dose at which these effects occurred in animal tests.

When spirotetramat was given to pregnant animals, effects on the developing fetus were observed at doses that were toxic to the mother, indicating that the fetus is not more sensitive to spirotetramat than the adult animal. In light of uncertainty with regards to whether the alterations in thyroid hormones and brain effects observed in adult animals could translate into adverse effects on the developing fetus, extra protective measures were applied during the risk assessment to further reduce the allowable level of human exposure to spirotetramat.

Residues in Water and Food

Dietary risks from food and water are not of concern

Refined aggregate dietary intake estimates (food plus water) revealed that the general population and children, the subpopulation that would ingest the most spirotetramat relative to body weight, are expected to be exposed to less than 20.5% of the acceptable daily intake. Based on these estimates, the chronic dietary risk from exposure to spirotetramat residues is not of concern for any of the population subgroups.

A single dose of spirotetramat is not likely to cause acute health effects in the general population (including infants and children). An aggregate (food and water) dietary exposure estimate of 1.1% of the acute reference dose is not considered to be a health concern for any of the population subgroups.

The *Food and Drugs Act* prohibits the sale of adulterated food, that is, food containing a pesticide residue that exceeds the established maximum residue limit (MRL). Pesticide MRLs are established under the authority of the *Food and Drugs Act* through the evaluation of scientific data under the *Pest Control Products Act*. Food containing a pesticide residue that does not exceed the established MRL does not pose an unacceptable health risk.

Residue trials conducted in representative NAFTA geographical locations on various crops using end-use products containing spirotetramat were acceptable. The residue trials were conducted in or on potatoes (Crop Subgroup 1C), grapes (Crop Subgroup 13-07F), Brassica vegetables (Crop Subgroups 5A and 5B), cucurbits (Crop Group 9), leafy vegetables, except Brassica (Crop Group 4), fruiting vegetables (Crop Group 8), hops,

pome fruits (Crop Group 11), stone fruits (Crop Group 12), and tree nuts (Crop Group 14). Residue data from European residue trials on dry bulb onions and strawberries, as well as citrus (Crop Group 10) from representative NAFTA geographical locations are sufficient to establish the proposed import maximum residue limits. The MRLs for this active ingredient can be found in the Science Evaluation.

Occupational Risks From Handling Movento 150 OD Insecticide and Movento 240 SC Insecticide.

Occupational risks are not of concern when Movento 150 OD Insecticide and Movento 240 SC Insecticide are used according to label directions, which include protective measures.

Farmers and pesticide applicators mixing, loading or applying Movento 150 OD Insecticide and Movento 240 SC Insecticide as well as field workers re-entering freshly treated fields can come in direct contact with Movento 150 OD Insecticide and Movento 240 SC Insecticide on the skin or through inhalation of spray mists. Therefore, the label will specify that anyone mixing or loading Movento 150 OD Insecticide and Movento 240 SC Insecticide must wear a long-sleeved shirt, pants and chemical-resistant gloves and that anyone applying the product must wear a long-sleeved shirt and pants. Taking into consideration these label requirements and that occupational exposure is expected to be short-term because this insecticide is applied only a couple of times per year, risk to farmers, applicators or workers is not a concern.

For bystanders, exposure is expected to be much less than that of field workers and is considered negligible. Therefore, health risks to bystanders are not of concern.

For people who enter treated fields for "pick-your-own" activities, exposure is expected to be short-term since this activity normally only happens once per year. Taking into consideration the label requirements, the risk to people that enter treated fields to pick produce is not a concern.

Environmental Considerations

What Happens When Spirotetramat Is Introduced Into the Environment?

Environmental risks are not of concern when Movento 150 OD Insecticide and Movento 240 SC Insecticide are used according to label directions, which include precautionary label statements and buffer zones.

Spirotetramat is non-persistent in soil and in water, with biotransformation being an important route of transformation. In aquatic systems under alkaline conditions, hydrolysis and phototransformation may also contribute to the dissipation of spirotetramat. Based on the physical and chemical properties of spirotetramt, it is not expected that this compound will leach through the soil profile and contaminate groundwater. Major transformation products in soil and water have been identified and

are discussed in the Science Evaluation section of this document. Residues of spirotetramat are not expected to be present in air due to its low volatility.

Use of spirotetramat does not present a risk to earthworms, small mammals, birds or aquatic organisms. However, spirotetramat may pose a risk to honeybee broods, beneficial arthropods and non-target plants. Precautionary label statements are thus included on the label and buffer zones of one to two metres are required to mitigate exposure of sensitive terrestrial habitats from spray drift.

Value Considerations

What Is the Value of Movento 150 OD Insecticide and Movento 240 SC Insecticide?

Movento 150 OD Insecticide and Movento 240 SC Insecticide control a variety of pests and can be used on a broad range of crop groups.

A single application of Movento 150 OD Insecticide or Movento 240 SC Insecticide provides control or suppression of a range of insect pests on a variety of fruit and vegetable crops. Use of this insecticide is compatible with current management practices and conventional crop production systems, and users are familiar with monitoring techniques to determine if and when applications are needed.

Other insecticides from the same class as spirotetramat are currently registered for use on some of the same crops as on the Movento labels; however, spirotetramat controls different pests and can be used on a broader range of crop groups. Prudent use of insecticides in this class should be observed to prevent the development of resistance. When applied according to label directions, Movento 150 OD Insecticide and Movento 240 SC Insecticide are effective in controlling whiteflies, mealybugs, some species of aphids, phylloxera, pear psylla, psyllids, San Jose scale, Lecanium scale (suppression only) and white peach scale.

Measures to Minimize Risk

Labels of registered pesticide products include specific instructions for use. Directions include risk-reduction measures to protect human and environmental health. These directions must be followed by law.

The key risk-reduction measures being proposed on the labels of Movento 150 OD Insecticide and Movento 240 SC Insecticide to address the potential risks identified in this assessment are as follows.

Key Risk-Reduction Measures

- **Human Health**

Since there is a concern with users coming into direct contact with spirotetramat on the skin or through inhalation of spray mists, anyone mixing/loading and involved in clean-up or repair activities with Movento 150 OD Insecticide and Movento 240 SC Insecticide must wear a long-sleeved shirt, pants and chemical-resistant gloves. In addition, anyone applying the products must wear a long-sleeved shirt and pants.

- **Environment**

To protect bees and beneficial arthropods, precautionary label statements are included on the Movento 150 OD Insecticide and Movento 240 SC Insecticide labels. To protect non-target terrestrial plants, Movento 150 OD Insecticide and Movento 240 SC Insecticide cannot be sprayed within one to two metres of sensitive terrestrial habitats. The distance allowed depends on the type of spray equipment used and the timing of application.

Next Steps

Before making a final registration decision on spirotetramat, the PMRA will consider all comments received from the public in response to this consultation document. The PMRA will accept written comments on this proposal up to 45 days from the date of publication of this document. In order to comply with Canada's international trade obligations, a period of 75 days from the date of publication of this document will be provided specifically for comments in regard to the proposed MRLs. Please forward all comments to Publications (contact information on the cover page of this document). The PMRA will then publish a Registration Decision document, which will include its decision, the reasons for it, a summary of comments received on the proposed final decision and the Agency's response to these comments.

Other Information

At the time the PMRA makes its registration decision, it will publish a Registration Decision document on spirotetramat (based on the Science Evaluation of this consultation document). In addition, the test data referenced in this consultation document will be available for public inspection, upon application, in the PMRA's Reading Room (located in Ottawa).

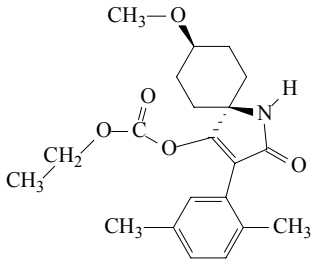
Science Evaluation

Spirotetramat

1.0 The Active Ingredient, Its Properties and Uses

1.1 Identity of the Active Ingredient

Active substance	Spirotetramat
Function	Insecticide
Chemical name	
1. International Union of Pure and Applied Chemistry (IUPAC)	cis-4-(ethoxycarbonyloxy)-8-methoxy-3-(2,5-xylyl)-1-azaspiro[4.5]dec-3-en-2-one
2. Chemical Abstracts Service (CAS)	cis-3-(2,5-dimethylphenyl)-8-methoxy-2-oxo-1-azaspiro[4.5]dec-3-en-4-yl ethyl carbonate
CAS number	203313-25-1
Molecular formula	$C_{21}H_{27}NO_5$
Molecular weight	373.45 g/mol
Structural formula	



Nominal purity of the active ingredient	97.37% (limits: 96%–100%)

1.2 Physical and Chemical Properties of the Active Ingredients and End-Use Product

Technical Product—Spirotetramat Technical

Property	Result
Colour and physical state	White powder
Odour	No characteristic odour
Melting point	142°C
Boiling point or range	N/A
Specific gravity at 20°C	1.23
Vapour pressure	Extrapolated 5.6×10^{-9} Pa at 20°C 1.5×10^{-8} Pa at 25°C 1.5×10^{-6} Pa at 50°C
Henry's law constant at 20°C	At pH 4: 6.24×10^{-8} Pa × m^3 × mol^{-1} At pH 7: 6.99×10^{-8} Pa × m^3 × mol^{-1} At pH 9: 1.09×10^{-7} Pa × m^3 × mol^{-1}
Ultraviolet (UV)-visible spectrum	**Peak maxima** (nm): 211, 276 **Molar absorptivity** (1000 cm^2/mol): 22.0×10^3, 0.8×10^3
Solubility in water	**pH**: 4, 7, 9 **Solubility (mg/L at 20°C)**: 33.5, 29.9, 19.1 In distilled water **pH**: 6.0–6.3 **Solubility (mg/L at 20°C)**: 33.4
Solubility in organic solvents at 20°C (g/100 mL)	**Solvent** / **Solubility (g/L at 20°C)**: Ethanol: 44 n-hexane: 0.055 toluene: 60 dichloromethane: >600 acetone: 100–120 ethyl acetate: 67 dimethyl sulfoxide: 200–300
n-Octanol−water partition coefficient (K_{ow})	**pH**: 4, 7, 9 **log K_{ow}**: 2.51, 2.51, 2.50 **K_{ow}**: 324, 324, 316
Dissociation constant (pK_a)	pK_a = 10.7

Property	Result
Stability (temperature, metal)	Thermally stable at ambient temperature under air. No exothermic reaction occurred between the melting point and decomposition temperature of 235°C. Stable in presence of metals and metal ions.

End-Use Products—Movento® 150 OD Insecticide and Movento® 240 SC Insecticide

Property	Movento® 240 SC Insecticide	Movento® 150 OD Insecticide
Colour	White	Light brown
Odour	Aromatic	Weak mouldy odour
Physical state	Liquid	Liquid
Formulation type	Suspension	Suspension
Guarantee	240 g/L (limits: 233–248 g/L)	150 g/L (limits: 142–158 g/L)
Container material and description	Plastic: 1 L to 200 L	Plastic jug or tote, 1 L to 200 L
Specific gravity	1.075 at 20°C	0.9993 at 20°C
pH of 1% dispersion in water	4.6	4.5
Oxidizing or reducing action	No oxidizing properties	The product does not contain any oxidizing or reducing agents.
Storage stability	The product was shown to be stable when stored for 2 weeks at 54°C. A one-year storage stability study is in progress.	The product was shown to be stable when stored for 2 weeks at 54°C in HDPE containers. A 1-year storage stability study is in progress.
Explodability	The product is not explosive.	The product is not explosive.

1.3 Directions for Use

Movento 150 OD Insecticide and 240 SC Insecticide are for use on grapes (excluding table grapes) and small fruit vine crops (Crop Subgroup 13F), pome fruits (Crop Group 11), stone fruits (Crop Group 12), tree nuts (Crop Group 14), hops, cucurbits (Crop Group 9), fruiting vegetables (Crop Group 8), leafy vegetables – both *Brassica* and non-*Brassica* (Crop Groups 4 and 5), and tuberous and corm vegetables (Crop Subgroup 1C) to control a variety of sucking insects. The application rate varies depending on the insect pest (Table 1.3.1). The product is applied as a foliar treatment by ground equipment only.

Table 1.3.1 Insect Control Claims for Movento 150 OD Insecticide and 240 SC Insecticide

Crop	Pest	Rate (g a.i./ha)	Maximum amount of a.i. per hectare per year
Crop Group 13F: Grapes (excluding table grapes) and small fruit vine climbing	Whiteflies	88–105	Maximum of 220 g a.i./ha
	Mealybugs Phylloxera Lecanium scale (suppression)	88–140	
Crop Group 11: Pome Fruits	Rosy apple and Apple aphids Whiteflies	88–105	Maximum of 440 g a.i./ha
	Pear psylla	88–105	
	Mealybugs San Jose scale	88–140	
Crop Group 12: Stone Fruits	Aphids Whiteflies	88–105	Maximum of 270 g a.i./ha
	Mealybugs San Jose scale White peach scale	88–140	
	Lecanium scale (suppression)		
Crop Group 14: Tree Nuts	Aphids Phylloxera Whiteflies	88–105	Maximum of 380 g a.i./ha
	Mealybugs San Jose scale Walnut scale	88–140	
	Lecanium scale (suppression)		
Hops	Hop aphid	88–105	Maximum of 220 g a.i./ha
Crop Group 9: Cucurbit Vegetables	Aphids Whiteflies	52–88	Maximum of 175 g a.i./ha
Crop Group 8: Fruiting Vegetables	Aphids Whiteflies Psyllids	52–88	Maximum of 175 g a.i./ha
Crop Group 4: Leafy Vegetables - Non *Brassica*	Aphids Whiteflies	52–88	Maximum of 175 g a.i./ha

Crop	Pest	Rate (g a.i./ha)	Maximum amount of a.i. per hectare per year
Crop Group 5: Leafy Vegetables - *Brassica*	Aphids Whiteflies	52–88	Maximum of 175 g a.i./ha
Crop Group 1C: Tuberous and Corm Vegetables	Aphids Whiteflies Psyllids	52–88	Maximum of 175 g a.i./ha

1.4 Mode of Action

Spirotetramat is proposed for classification as a Group 23 Insecticide, the tetronic acid derivatives. These compounds are believed to be inhibitors of lipid synthesis. Spirotetramat is a systemic insecticide with a limited spectrum, targeting Homopteran insects.

2.0 Methods of Analysis

2.1 Methods for Analysis of the Active Ingredient

The methods provided for the analysis of the active ingredient and the impurities in Spirotetramat Technical Insecticide have been validated and assessed to be acceptable for the determinations.

2.2 Method for Formulation Analysis

The methods provided for the analysis of the active ingredient in the formulations have been validated and assessed to be acceptable for use as enforcement analytical methods.

2.3 Methods for Residue Analysis

2.3.1 Multiresidue Methods for Residue Analysis

Spirotetramat (BYI 08330), BYI 08330-enol, BYI 08330-ketohydroxy, BYI 08330-mono-hydroxy, BYI 08330-enol-glucoside (Glc), and BYI 08330-enol-glucuronide (GA) were screened through multiresidue methods described in the United States Food and Drug Administration (FDA) Pesticide Analytical Manual, Vol. I (PAM I). Spirotetramat and the metabolites were tested for natural fluorescence using procedures outlined in Protocol A of PAM I. BYI 08330-mono-hydroxy was the only compound found to be naturally fluorescent; no further test with this protocol was performed. Spirotetramat and the metabolites were subjected to Protocol C, modules DG1, DG5, DG13, DG17 and DG18. Due to the poor sensitivity of the test substances to detection by methods described in Protocol C, no further analyses were performed for Protocols D, E or F. Since the test substances are not acidic, phenols or substituted ureas, analyses were not performed using Protocols B or G. Therefore, the multiresidue methods

are not adequate for the enforcement of MRLs for spirotetramat and the relevant metabolites. Methods for residue analysis are summarized in Appendix I, Table 1.

2.3.2 Methods for Residue Analysis of Plant and Plant Products

A reverse phase high-performance liquid chromatography–electrospray ionization with tandem mass spectrometry (LC-MS/MS) method was developed for the analysis of spirotetramat and the metabolites BYI 08330-enol, BYI 08330-ketohydroxy, BYI 08330-mono-hydroxy and BYI 08330-enol-glucoside (Glc) in food of plant origin for data gathering (00857) and enforcement purposes (01084). Both methods fulfilled the requirements with regards to specificity, accuracy and precision at the method limit of quantitation. A limit of quantitation was reported as 0.01 ppm in plant products, and 0.1 ppm in hop cones for each analyte. The limit of detection (LOD) for each analyte was estimated to be 0.003 ppm for all matrices except for hop cones (0.03 ppm). Acceptable recoveries (70–120%) of spirotetramat and the metabolites were obtained in plant matrices. Extraction efficiency data demonstrated that the enforcement method can account for incurred residues of spirotetramat and the metabolites in cotton gin trash, lettuce and apples.

An LC-MS/MS method (00929) was also developed for the determination of the residues of BYI 08330-ketohydroxy-alcohol, BYI 08330-desmethyl-ketohydroxy and BYI 08330-desmethyl-di-hydroxy in rotational crops. This method fulfilled the requirements with regards to specificity, accuracy and precision at the method limit of quantitation. A limit of quantitation was reported as 0.02 ppm for each analyte in the rotational crops. Acceptable recoveries (70–120%) of spirotetramat and the metabolites were obtained in plant matrices (wheat, cotton, Swiss chard, peanut, sugar beets). Extraction efficiency data demonstrated that the enforcement method can account for incurred residues of spirotetramat and the metabolites in Swiss chard and wheat straw. Methods for residue analysis are summarized in Appendix I, Table 1.

2.3.3 Methods for Residue Analysis of Food of Animal Origin

A reverse phase high-performance liquid chromatography–electrospray ionization with tandem mass spectrometry (LC-MS/MS) method (00966) was developed for the determination of residues of spirotetramat and the metabolites BYI 08330-enol and BYI 08330-enol-glucuronide (GA) in livestock matrices. A similar method (00969) was developed for enforcement purposes for the determination of residues of spirotetramat and the metabolite BYI 08330-enol. These methods fulfilled the requirements with regards to specificity, accuracy and precision at the method limit of quantitation. A limit of quantitation of 0.01 ppm was demonstrated for each analyte in livestock matrices (tissues and eggs) and 0.005 ppm for milk. Acceptable recoveries (70–120%) of spirotetramat and the metabolites were obtained in livestock matrices. Extraction efficiency data was not considered necessary since the enforcement method used the same extraction solvent as the livestock metabolism study. Methods for residue analysis are summarized in Appendix I, Table 1.

2.3.4 Methods for Residue Analysis in Soil, Water, Sediment and Air

High-performance liquid chromatography methods with tandem mass spectrometry (HPLC-MS/MS) were developed and proposed for data generation and enforcement purposes. These methods fulfilled the requirements with regards to selectivity, accuracy and precision at the respective method limit of quantitation. Acceptable recoveries (70–120%) were obtained in plant and animal matrices and environmental media. Methods for residue analysis are summarized in Appendix I, Table 1.

3.0 Impact on Human and Animal Health

3.1 Toxicology Summary

A detailed review of the toxicological database for spirotetramat was conducted. The database is complete, consisting of the full array of toxicity studies currently required for hazard assessment purposes. The studies were carried out in accordance with currently accepted international testing protocols and Good Laboratory Practices. The scientific quality of the data is high and the database is considered adequate to define the majority of the toxic effects that may result from exposure to this chemical pest control product.

Spirotetramat was of low acute toxicity by the oral, dermal and inhalation routes of exposure in Wistar rats. It was non-irritating when applied to the skin and moderately irritating to the eyes of Himalayan rabbits. Spirotetramat was positive for skin sensitization using the Guinea Pig Maximization and Local Lymph Node Assay methods.

Movento 150 OD Insecticide formulation was of low acute toxicity via the oral and dermal routes and was slightly toxic via the inhalation route in Wistar rats. It was mildly irritating when applied to the skin and severely irritating when instilled into the eyes of New Zealand White rabbits. Results of skin sensitization testing in guinea pigs using the Buehler method were positive.

Movento 240 SC Insecticide formulation was of low acute toxicity via the oral, dermal and inhalation routes in Wistar rats. It was non-irritating when applied to the skin and minimally irritating when instilled into the eyes of New Zealand White rabbits. Results of skin sensitization testing in guinea pigs using the Buehler method were positive.

Four metabolites in plants (BYI 08330-cis-ketohydroxy, BYI 08330-desmethyl-ketohydroxy, BYI 08330-di-hydroxy and BYI 08330-mono-hydroxy) were also assessed and found to be of low acute toxicity via the oral route in supplementary studies conducted with rats.

The pharmacokinetic behaviour of spirotetramat was characterized by rapid absorption and elimination from the plasma in rats. Absorption was extensive with between 89 and 98% of the total recovered radioactivity excreted via the renal route. No significant differences in absorption rate were observed between sexes, or between low dose, high dose, or repeated low dose tests. Urinary excretion was rapid and was the major route of elimination (88–95% of Administered Dose (AD)) for both sexes and all dose regimens. Fecal elimination accounted for 2 to 11% of the AD. Excretion was nearly complete within 24 to 48 hours. Expired air was not assessed for

spirotetramat concentration; however, nearly all of the administered test substance was accounted for in the urine and feces.

Spirotetramat was completely metabolized in the rat. The main metabolic reaction was cleavage of the ester group resulting in the most prominent metabolite, BYI08330-enol (53-87% of AD). All other metabolites could be derived from the enol intermediate. The second most prominent metabolite was BYI08330-desmethyl-enol (5–37% of AD), resulting from oxidative demethylation of the 8-methoxy group. Four more identified metabolites were of minor importance: BYI08330-ketohydroxy, BYI08330-desmethyl-ketohydroxy, BYI08330-enol-glucuronide (GA) and BYI08330-enol-alcohol. A sex-related difference was noted in the quantitative distribution of the two main metabolites, with male rats showing much higher rates of demethylation of BYI08330-enol to BYI08330-desmethyl-enol than female rats. Quantitative whole body autoradiography analysis identified the highest concentrations of spirotetramat and its metabolites in the liver, kidney, gastrointestinal tract, urinary bladder and blood. Tissue levels were generally higher for females than males.

Spirotetramat inhibits Acetyl CoA Carboxylase, a key enzyme in fatty acid biosynthesis. The biological activity of cyclic ketoenols in treated insects results in decreased lipid contents, notably triglycerides and free fatty acids. The insecticidal mode of action was not reflected in repeat dosing 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.

Following repeated dosing in the dog, treatment-related declines in circulating thyroid hormones (T_4 and/or T_3) were observed at doses of 20/19 mg/kg bw/day (males/females) and above. In addition, decreased size of peripheral thyroid follicles was noted in two out of four males at the highest dose (55 mg/kg bw/day) in the 12-month study. With the exception of these findings, there were no changes to thyroid weight or histopathology in either sex. Thyroid stimulating hormone (TSH) serum levels appeared to be decreased in only the 28-day dog study; however, these results were based on only two animals/sex/dose. The thyroid hormone findings were considered to reflect a response to treatment with spirotetramat, although interpretation was hampered somewhat due to variability in the data as well as the limitations of working with data based on small group sizes. Nonetheless, evidence of effects on thyroid hormones was recorded in all the dog studies, which spanned 28 days to 12 months. These thyroid hormone effects, although treatment-related, were considered non-adverse in the adult dog. There was limited information as to the dosing duration required to elicit changes to thyroid hormones in the dog studies, due to the protocol sampling intervals as well as the somewhat limited group sizes. The 28-day study suggested that the changes could be produced following one week of dosing on the evidence obtained from only two dogs/sex/dose. When compared to the results following more extended dosing duration, however, the data suggested that a relatively higher level of spirotetramat was required to effect such changes. Thymus effects, characterized by atrophy and increased incidence of involution were also noted in all dog studies, appearing at lower doses when dose duration was extended. Dilatation of cerebral ventricles was evident in both sexes at the mid-dose in the 12-month dog study, with additional effects occurring at higher doses (slight multifocal vacuolization of white matter; and slight focal hemorrhage of ventricle and axonal degeneration). Evidence of neurotoxicity was also observed, characterized by decreased activity/reactivity, whole body seizures and ataxia. The thymus and brain effects were considered to be the most sensitive endpoints in the database and were observed at dose levels as

low as 19 mg/kg bw/day following 12 months of dosing. Overall, the lowest no-observed adverse effect level (NOAEL) for these effects was 5 mg/kg bw/day from the 12-month dietary study in the dog.

In repeated oral dosing studies in rats, the primary target organs were the lungs, testes, kidneys and liver. The predominant findings in the lungs were an increased incidence of accumulation of alveolar macrophages in both sexes at doses of 189 mg/kg bw/day and greater, combined with an increased incidence of discolouration of the lung, decreased lung weight and progression to interstitial pneumonia at higher doses. The severity of these effects appeared to increase with duration of dosing. Testis effects included abnormal spermatozoa, hypospermia and an increase in exfoliated germ cell/debris in the epididymis, as well as decreased testicular weight, increased incidence of slight morphological change and testicular degeneration (tubular degeneration, vacuolation). The severity and type of findings were similar regardless of dosing duration and occurred at doses of 373 mg/kg bw/day and above. An additional group from the 90-day study receiving 616 mg/kg bw/day was observed over a four-week recovery period after cessation of dosing. Following the recovery period, the incidence and severity of testis effects in this group closely resembled that of the untreated control group. Kidney effects were noted in the two-year study only and were characterized by a decrease in absolute kidney weight combined with an increase in renal tubular dilation at the mid-dose and above in both sexes. An increase in relative liver weight was noted in both sexes in the one-year study only. Females at the highest dose tested (HDT) in the two-year study displayed an increased incidence of liver hyperplasia/fibrosis with associated minimal periportal mononuclear cell infiltrate. In addition, declines in body weight and body weight gain were noted in high dose animals in all studies. Spirotetramat was not oncogenic in the rat. It is noteworthy that the thyroid and thymus findings that were observed in dogs were not observed in rats at any dose, while the testicular histopathology observed in rats as a result of administration of spirotetramat was not observed in dogs.

Effects noted in a supplemental study with rats treated with a high dose of the enol metabolite (800 mg/kg bw/day via gavage over 10 days) were limited to low food consumption and body weight gain. No control animals were available for comparison.

In mice, no adverse effects were observed following dietary dosing for 90 days as well as following 18 months of dietary administration. Spirotetramat was not oncogenic in the mouse.

Results from a comparative in vitro metabolism study using hepatocytes from male rats, mice and humans revealed some species differences in the proportion of spirotetramat metabolites formed. Specifically, mouse hepatocytes were better able than rat or human liver cells to metabolize BYI 08330-enol via glucuronidation. The metabolic profile generated from the human hepatocytes was more comparable to that of the mouse than of the rat. In both mouse and human tissue, conjugation was more prevalent than oxidative transformation. Results obtained from rat hepatocytes corresponded to in vivo metabolism findings in the rat. Dog hepatocytes were not included in this study; therefore, comparison to findings in other species could not be made.

Dermal dosing of rats for 28 days yielded no evidence of systemic toxicity when spirotetramat was tested up to 1000 mg/kg bw/day.

With respect to genotoxic potential, a weak positive finding was noted in a single in vitro chromosomal aberration test, but at cytotoxic concentrations only. Negative findings were recorded in two in vivo chromosomal aberration studies and one in vivo/in vitro unscheduled DNA synthesis assay using rat hepatocytes. The overall evidence did not suggest that spirotetramat was genotoxic.

In an acute rat neurotoxicity study, a decrease in locomotor activity as well as interval locomotor activity was noted in treated males on the day of dose administration. Effects were noted at 200 mg/kg bw, the lowest dose tested. A follow-up study was conducted to confirm results and establish a NOAEL of 100 mg/kg bw for this endpoint. There was no evidence of neurotoxicity in a functional observation battery performed on 10 animals per dose in the one-year rat study. In dogs, however, repeated dosing resulted in clinical signs of neurotoxicity as well as neuropathology, as previously noted.

The reproductive toxicity potential of spirotetramat was assessed in a one-generational range-finding and a multigenerational reproductive toxicity study in rats. In the two-generation reproductive toxicity study, parental effects at the high dose in both parental (P) and first filial (F_1) generations included decreased body weight and body weight gain during pre-mating, gestation and lactation, decreased food consumption during lactation and tubular dilation of the kidneys combined with decreased kidney weight. Offspring toxicity characterized by a decrease in body weight and body weight gain during lactation was noted in both F_1 and F_2 pups at the high dose. A transient decrease in body weight gain occurred in F_2 pups at this dose as well as at the next lower dose (71/83 mg/kg bw/day) around weaning, at which time the pups were beginning to consume the diet and therefore receiving a higher intake on a mg/kg bw/day basis. Development of the sexual organs of the offspring (balano-preputial separation, vaginal opening) was unaffected by treatment. High dose F_1 males had a higher incidence of abnormal sperm cells (sperm with amorphous heads) and one male in this group experienced a decline in fertility, indicating that spirotetramat demonstrated reproductive toxicity in males. In the one-generation reproductive toxicity study, decreased sperm motility and progression, decreased epididymal sperm counts and a lack of pregnancy and absence of implantation sites in dams were noted in animals treated with doses up to 538/646 mg/kg bw/day. In this study, no effects on developmental landmarks were noted in a subset of F_1 males that were maintained until week 9; however, effects on sperm were observed in these individuals at a lower dose than in the P generation.

These effects on sperm were observed in both the one-generation and two-generation reproductive toxicity studies. Effects on male reproductive function and performance triggered several mechanistic studies and pharmacokinetic investigations.

In an investigative study designed to explore the time of onset of testicular toxicity in rats, animals were dosed by gavage with spirotetramat, and sperm was sampled at 3, 10, 21 or 41 days. Decreased epididymal sperm counts were recorded following 10 days of treatment with 1000 mg/kg bw/day. No adverse effects on sperm counts were observed following three days of treatment. Repeated dosing is therefore necessary to produce male reproductive toxicity in rats. In a second investigative 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. These

findings suggest that male reproductive toxicity in rats is likely due to the enol metabolite of spirotetramat (or a derivative thereof) rather than the parent compound.

Developmental toxicity was assessed in rats and rabbits. In rats, a second developmental toxicity study was conducted to further elucidate the low-dose findings of the first (main) study. Fetal toxicity was observed in the presence of maternal toxicity in rats only. In rats, reduced fetal weight and increased incidence of malformations and skeletal deviations were observed at 1000 mg/kg bw/day. Malformations at the high dose included single cases of cleft palate, co-arctation of aortic arch, atrial septal defect of the heart, microphthalmia, and supernumerary lumbar vertebra, four cases of dysplastic forelimb bones, and three cases of malformed sacral vertebral arch with pelvic shift. Skeletal findings at this dose consisted of incomplete or delayed ossification and variations. Maternal toxicity at the same dose consisted of clinical signs of toxicity (respiratory effects), and decreased food consumption, body weight and body weight gain. Increased incidences of wavy ribs and retarded ossifications at lower doses in the main rat study were without dose response on a litter basis. In addition, delays in ossification seen in multiple sites in the main study were not reproducible at the same or lower doses in the supplementary rat developmental toxicity study. A combined developmental NOAEL for these two studies was therefore set at 140 mg/kg bw/day based on effects seen at the high dose only. These studies suggest a qualitative sensitivity of the young for effects occurring at the limit dose of testing.

In the developmental toxicity study in rabbits, maternal toxicity was observed at doses of 40 mg/kg bw/day and above, including a dose-dependent increase in abortion and other clinical signs of toxicity in affected animals. Abortion occurred in one dam at 40 mg/kg bw/day and two dams at the highest dose (160 mg/kg bw/day) and was always preceded with clinical signs indicative of pronounced toxicity in affected females, including severe body weight loss. An additional six dams at the high dose were either found dead or sacrificed moribund between gestation day 15 and 28. There was no indication of developmental toxicity in the rabbit. A range-finding study in rabbits produced similar results, although abortions were not observed until animals were dosed with 250 mg/kg bw/day and higher. Dose groups in the range-finding study were limited to three dams per dose, however, so it was not expected that abortion, which occurred in 1 out of 22 females at 40 mg/kg bw/day in the main study, would be noted in such a limited number of animals. In both studies, abortions did not occur until gestation day 22 to 26, indicating that repeat dosing is necessary to elicit this response.

Overall, spirotetramat was not carcinogenic or genotoxic. Spirotetramat was not teratogenic in rabbits and was teratogenic in rats only at maternally toxic doses. There was variability in toxicological response among test species, which may reflect differences in metabolism. Mice were relatively insensitive to the test substance, whereas adverse effects were observed in the rat and the dog. In the rat, males appeared to be more sensitive to spirotetramat toxicity than females, with the male reproductive system (sperm, testes and epididymides) identified as a target for toxicity. Sperm toxicity was noted in the F_1 males at lower doses than in the P-generation males. The most sensitive test species appeared to be the dog, as evidenced by thymus and central nervous system effects as well as perturbations in thyroid hormones. The decrease in thyroid hormone levels was a consistent finding in all dog studies. There was evidence of clinical signs of neurotoxicity as well as brain pathology in the dog. These signs defined the lowest NOAEL in the database. The implications of the thyroid and brain findings in

adult dogs as they relate to neuroendocrine development of the young animal were taken into account in the risk assessment.

Results of the acute and chronic tests conducted on laboratory animals with spirotetramat and its associated end-use products, along with the toxicology endpoints for use in the human health risk assessment, are summarized in Appendix I, Tables 2, 3 and 4.

3.1.1 PCPA Hazard Characterization

For assessing risks from potential residues in food or from products used in or around homes or schools, the *Pest Control Products Act* requires the application of an additional 10-fold factor to take into account completeness of the data with respect to the exposure of, and toxicity to, infants and children, as well as potential prenatal and postnatal toxicity. A different factor may be determined to be appropriate on the basis of reliable scientific data.

With respect to the completeness of the toxicity database, extensive data were available for spirotetramat, including prenatal developmental toxicity studies in rats and rabbits, as well as one- and two-generation reproduction studies.

With respect to potential prenatal and postnatal toxicity, the prenatal developmental toxicity studies in rats and rabbits provided no quantitative indication of increased susceptibility of rat or rabbit fetuses to in utero exposure to spirotetramat relative to the adult. Malformations in rats were noted at the limit dose and were accompanied by maternal toxicity. Decreased motility and progression, and an increase in the number of abnormal sperm were noted in F_1 males in the absence of similar findings at the same dose level in the parental animals. Attainment of developmental landmarks in rat offspring receiving in utero as well as early postnatal exposure was not adversely affected.

In rats, there was no indication of clinical signs of neurotoxicity or neuropathology following one year of treatment. In the acute neurotoxicity study in the rat, clinical signs of neurotoxicity were limited to a decrease in locomotor activity for males, only on the day of dosing. In adult dogs, however, brain pathology and effects on thyroid hormones were observed following repeated dosing. Rodents did not demonstrate findings indicative of thyroid toxicity. In both dogs and humans, thyroxine (T_4) is bound to the transport protein thyroxine binding globulin (TBG), with humans exhibiting a higher degree of thyroxine binding than dogs (and subsequently, the least amount of unbound serum T_4). This protein is not present in rodents (transthyretin is the major T_4 transport protein in plasma of rodents). For this reason, the dog is a relevant model for human health risk assessment. The possible impact of the observed thyroid hormone perturbation to a developing fetus and the young is not known as the available dog studies were conducted in adult animals. As thyroid toxicity was not observed in the rat, the rat developmental and reproductive toxicity studies, or for that matter, a developmental neurotoxicity (DNT) study, would not address this concern. As a point of note, changes in thyroid hormones have been observed in dogs after dosing with other insecticides in this class (acid ketoenol). In those cases, thyroid hormone toxicity was also observed in rats, enabling the rat to be used as an appropriate species for risk assessment.

In light of the thyroid findings in adult dogs and the role of the thyroid in development of neurological and reproductive systems in the young, there is residual uncertainty with respect to the completeness of the toxicology database as it relates to prenatal and postnatal toxicity. With regards to the overall level of concern for the thyroid findings, the following information should be noted. All of the required studies relevant to assessing risks to infants and children were available for this assessment (DNT study would not address concerns as noted previously). Malformations (at maternally toxic doses) and sperm effects were observed at dose levels that were significantly higher than the doses producing effects in dogs (clinical signs of neurotoxicity and brain pathology); these effects in dogs generated the lowest NOAEL in the database. In addition, although thyroid hormones were affected in all three dog studies, there was a lack of correlative overt thyroid toxicity with considerable variability in the thyroid hormone data. All of these considerations serve to lower the level of concern that has been raised for repeated dosing scenarios. Therefore, for such scenarios, it was considered appropriate to retain the PCPA factor, but that it could be reduced from the default value (see Sections 3.2 and 3.3).

3.2 Determination of Acute Reference Dose

The recommended acute reference dose (ARfD) for spirotetramat is 1 mg/kg bw, calculated using the NOAEL of 100 mg/kg bw from the acute neurotoxicity study in rats. This NOAEL was based on a decrease in locomotor activity observed at the next highest dose (LOAEL = 200 mg/kg bw). The standard uncertainty factor of 100 is required to account for interspecies extrapolation (10-fold) as well as intraspecies variability (10-fold). With respect to the PCPA factor, uncertainty regarding the possible impact of the observed thyroid hormone perturbation to a developing fetus was not considered to be relevant in the context of a single dose exposure. Therefore, the PCPA factor can be reduced from 10-fold to 1-fold.

The ARfD is calculated to be 100 ÷ 100 = 1 mg/kg bw and is considered to be protective of all populations, including infants and children.

3.3 Determination of Acceptable Daily Intake

The recommended acceptable daily intake (ADI) for spirotetramat is 0.02 mg/kg bw/day based on the NOAEL of 5 mg/kg bw/day in the 12-month dietary dog study. This NOAEL was based on brain effects (dilatation of brain ventricle) in both sexes and thymus effects (increased involution and decreased thymus size) in males at 19/20 mg/kg bw/day (in M/F), and is the lowest NOAEL in the database. Decreased thyroid hormones (T_4) were also observed at this dose level. The standard uncertainty factor of 100 is required to account for interspecies extrapolation (10-fold) as well as intraspecies variability (10-fold). With respect to the PCPA factor, all of the required studies relevant to assessing risks to infants and children were available for this assessment. For the reasons outlined in the PCPA Hazard Characterization Section, it was considered appropriate to retain the PCPA factor, but that it could be reduced from 10-fold to 3-fold. The approach taken in evaluating the information is consistent with that applied for other products in this chemical class with similar concerns. The PCPA 3-fold factor was added to the standard 100-fold, resulting in a composite assessment factor of 300 in the calculation of the ADI.

The resulting ADI is 5 ÷ 300 = 0.02 mg/kg bw/day, and is considered to be protective of all populations, including infants and children. The ADI is protective of other toxicity endpoints observed in the database by the following margins: 3550-fold to the NOAEL for sperm toxicity in rats, 660-fold to the NOAEL for lung effects in rats, 625-fold to the NOAEL for kidney effects in rats, and 7000-fold to the NOAEL for malformations in rats.

3.4 Occupational and Bystander Risk Assessment

3.4.1 Toxicological Endpoints

Short- and intermediate-term inhalation and dermal exposure (to cover farmer mixers/loaders/ applicators, custom mixers/loaders/applicators and re-entry workers)

The NOAEL of 32 mg/kg bw/day from the 90-day dietary study in dogs is considered the most appropriate endpoint for use in the occupational and bystander risk assessment since no studies of appropriate duration conducted via the inhalation or dermal routes were available, and the dog was the most sensitive species in the database. This NOAEL is based on clinical signs of toxicity, decreases in body weight gain and food consumption, effects on hematological parameters and thymus atrophy. Non-adverse decreases in T_3 were also observed at the LOAEL. The worker population could include pregnant females. For this reason, the residual uncertainty with respect to the thyroid hormone effects and the possibility of effects in developing offspring is relevant, and an additional 3-fold uncertainty factor is considered appropriate. The target margin of exposure (MOE) is 300**,** accounting for standard uncertainty factors of 10-fold for interspecies extrapolation and 10-fold for intraspecies variability, as well as an additional 3-fold as noted above. The selection of this study and MOE is considered to be protective of all populations, including nursing infants and the unborn children of exposed female workers.

3.4.2 Dermal Absorption

In an in vivo rat study, the absorption, distribution and excretion (via urine and feces) of radioactivity was studied in male rats following a single dermal dose of ^{14}C-spirotetramat applied at nominal levels of 100, 15 or 5 µg/cm^2. A group of 16 animals were treated at each of the dose levels. Prior to washing of the dose site and animal sacrifice, the groups of animals underwent a post-exposure period in accordance with the following schedule:

Table 3.4.2.1 Schedule of Dermal Dose Exposure

Number of animals (16 animals total)	**4**	**4**	**4**	**4**
Duration of exposure (hours)	1	10	24	10
Sacrifice after (hours)	1	10	24	168

Mean recoveries of radioactivity from all dose groups were found to be acceptable in the range of 91.8 to 100.6% of the total radioactivity administered. The largest proportion of radioactivity was recovered from skin wash (surface of the skin). The mean relative amount of radioactivity absorbed (including urine, feces, cage wash, tissues/organs and carcass) showed a distinct time dependency where skin bound residues of ^{14}C-spirotetramat became systemically available over

time and was not influenced by the dose level. A maximum apparent absorption (systemic absorption and skin bound residues combined) of 17.62% was observed after 10 hours of exposure, based on the residues in the urine, feces, cage wash, blood cells, plasma, kidney, liver, carcass and residues found in the skin at the application site. The value of 17.62% was considered appropriate for use in the dermal exposure assessment.

3.4.3 Mixer, Loader and Applicator Exposure and Risk Assessment

Farmers and custom pesticide applicators may be exposed to Movento 150 OD Insecticide or Movento 240 Insecticide when mixing, loading or applying these products. Movento 150 OD Insecticide or Movento 240 SC Insecticide is applied at a range of 52 to 140 grams of active ingredient per hectare. A farmer can typically treat anywhere from 8 to 150 hectares per day using groundboom or airblast equipment and a custom applicator can typically treat from 16 to 300 hectares per day using the same equipment. A farmer may be exposed for two days per year, while a custom applicator may be exposed for up to a month over the course of a year.

Exposure estimates for mixers, loaders and applicators are based on data from the Pesticide Handlers Exposure Database (PHED), Version 1.1. PHED is a compilation of generic mixer/loader/applicator passive dosimetry data with associated software, which facilitates the generation of scenario-specific exposure estimates. Appropriate subsets of A and B grade data (high confidence) were created from the database files of PHED for liquid open mixing/loading, open cab airblast and open cab groundboom. All data were normalized for kilograms of active ingredient handled. Exposure estimates are presented on the basis of the best-fit measure of central tendency, i.e. summing the measure of central tendency for each body part that is most appropriate to the distribution of data for that body part. Exposure estimates are based on unit exposure values from the PHED, coupled with application rate and typical area treated per day inputs. The exposure estimates are based on mixers/loaders/applicators (M/L/A) wearing a single layer of clothing (long pants and a long-sleeved shirt), and in addition, mixers/loaders wearing gloves when using airblast and groundboom equipment. Exposure estimates for applicators were based on a single layer of clothing (no gloves) when using airblast and groundboom equipment. The estimated worker exposure was based on a worker body weight of 70 kg and dermal absorption of 17.62% for males and females.

For a farmer treating up to 150 hectares at the maximum label rate of 0.175 kg a.i./ha, the daily amount of active ingredient handled could be 15.75 kg a.i./day. A custom applicator would handle 31.50 kg a.i./day while treating 300 hectares.

For the short- to intermediate-term risk assessments, MOEs were generated based on the NOAEL of 32 mg/kg bw/day from the 90-day dietary study in dogs. All MOEs are above the target MOE of 300; therefore, they are considered acceptable (Table 3.4.3.1).

Table 3.4.3.1 Mixer/Loader/Applicator Exposure Summary

Scenario	Application Rate (g ai/ha)	ATPD (ha/day or L/day)	Amount of a.i. handled per day (kg a.i./day)[1]	Daily Exposure (dermal + inhalation) (µg ai/kg bw/day)[2]	MOE[3]
Farmer M/L/A	88–140	8–150	1.12–15.75	0.699–20.293	8182–45763
Custom M/L		16–300	2.24–31.50	0.34–4.77	6702–94243
Custom A				0.68–18.97	1687–46991

1 Amount of a.i. handled per day calculated using the application rate × Area Treated Per Day (ATPD)
2 Daily exposure was calculated using amount of a.i. handled per day × PHED unit exposure value/body weight (70kg); a default value of 17.62% dermal absorption was used.
3 Exposure estimates for custom M/L and custom applicator (intermediate-term) were compared to a NOAEL of 32 mg/kg bw/day established in the 90-day dietary toxicity study in dogs, target MOE = 300.

3.4.4 Bystander Exposure and Risk Assessment

Bystander exposure should be negligible because Movento 150 OD Insecticide or Movento 240 SC Insecticide is to be applied to agricultural crops when wind speeds do not exceed 16 km/hour. Therefore, the potential for drift to human habitation or to areas in which human activity occurs, such as houses, cottages, schools and parks, is expected to be minimal.

3.4.5 Exposure and Risk Assessment for Workers Entering Treated Crops

There is potential for exposure of workers entering treated fields to perform various activities, including hand harvesting, pruning, thinning, irrigating, weeding and scouting.

The duration of exposure is considered to be short- to intermediate-term, and the primary route of exposure for workers that enter treated crops would be dermal through contact with residues on the leaves. Inhalation exposure is expected to be negligible as the vapour pressure of spirotetramat is less than 1.5×10^{-10} mbar at 25°C, making it effectively non-volatile.

Dermal exposure to workers entering treated areas is estimated by coupling chemical-specific dislodgeable foliar residue values with activity-specific transfer coefficients. Activity transfer coefficients are based on Agricultural Re-entry Task Force data, of which Bayer CropScience Inc. is a member. Two chemical-specific dislodgeable foliar residue studies were submitted and found to be acceptable for use in exposure assessments. One study was conducted on hops and the other on grapes. A value of 0.203 µg/cm^2 was chosen from the hop study and will be used to estimate exposure on hops on the day of spraying. A value of 0.355 µg/cm^2 was chosen from the grape study for estimating exposure on all other crops on the day of spraying. For the risk estimates, exposure was compared with the NOAEL of 32 mg/kg bw/day from the 90-day dietary study in dogs. A dermal absorption value of 17.62% was used to estimate systemic exposure.

All margins of exposure are above the target MOE of 300; therefore, they are considered to be acceptable (Table 3.4.5.1). A 12-hour restricted-entry interval is required on the label for all agricultural crops.

Table 3.4.5.1 Postapplication Margin of Exposure

Scenario	Transfer Coefficient (cm^2/hr)[1]	Exposure Estimate (mg/kg bw/day)[2]	MOE[3]
Crop Group 1C: Tuberous and Corm Vegetables	2500	0.018	1791
Crop Group 4: Leafy Vegetables (except *Brassica* vegetables)	2500	0.018	1791
Crop Group 5: *Brassica* (Coles) Leafy Vegetables	5000	0.036	895
Crop Group 8: Fruiting Vegetables (except cucurbits)	1000	0.007	4476
Crop Group 9: Cucurbit Vegetables	2500	0.018	1791
Crop Group 11: Pome Fruits[4]	3000	0.043	746
Crop Group 12: Stone Fruits	3000	0.021	1492
Crop Group 13F: Berries	1500	0.011	2984
Grapes[5] (excluding table grapes)	8500	0.061	527
Hops[5]	2000	0.008	3914
	19300	0.079	406
Crop Group 14: Tree nuts	3000	0.021	1492

[1] Transfer Coefficients, based on ARTF data. The applicant, Bayer CropScience Inc., is a member of ARTF. Transfer coefficient values are as documented in USEPA Science Advisory Council for Exposure. Policy Number 003.1. 7 May 1998.

[2] Exposure estimates were calculated using the following formula:

$$\frac{\text{DFR Value } (\mu g/cm^2) \times \text{Transfer Coefficient } (cm^2/hr) \times \text{Hours Worked per Day (hr)} \times \text{Conversion Factor } (1mg/1000\mu g)}{\text{Body Weight (70 kg)}}$$

[3] NOAEL of 32 mg a.i./kg bw/day; target MOE of 300.

[4] 22 January 2004. Memo, TC for Orchard Tree Crops and Christmas Trees.

[5] 26 July 2005 Memo, TC for Grapes, Trellis Crops and Caneberries

3.5 Food Residues Exposure Assessment

3.5.1 Residues in Plant and Animal Foodstuffs

The residue definition for enforcement and risk assessment purposes in primary crops is spirotetramat (BYI 08330), BYI 08330-enol, BYI 08330-ketohydroxy, BYI 08330-mono-hydroxy and BYI 08330-enol-glucoside (Glc), expressed as BYI 08330 equivalents. The residue definition for enforcement purposes in animal commodities is spirotetramat and BYI08330-enol, expressed as BYI08330 equivalents. The residue definition for risk assessment purposes in animal commodities is spirotetramat, BYI08330-enol and BYI08330-enol-glucuronide, expressed as BYI08330 equivalents.

The data gathering and enforcement analytical methodologies, reverse phase high-performance liquid chromatography–electrospray ionization with tandem mass spectrometry (LC-MS/MS), are valid for the quantitation of the analytes of interest in plant and livestock commodities. The total residues of spirotetramat and the metabolites BYI 08330-enol, BYI 08330-ketohydroxy, BYI 08330-mono-hydroxy and BYI 08330-enol-glucoside (Glc) are stable in tomato (fruit and paste), potato (tuber), lettuce (head), climbing French bean (bean with pod) and almond (nutmeat) matrices when stored in a freezer at -18°C for up to 24 months (718 days). Total residues of spirotetramat were stable for up to five months (147 days) in orange juice and prunes.

Residue data from trials conducted in representative NAFTA growing regions on various crops using end-use products containing spirotetramat are sufficient to support the establishment of maximum residue limits. The residue trials were conducted in or on potatoes (Crop Subgroup 1C), grapes (Crop Subgroup 13-07F), *Brassica* vegetables (Crop Subgroups 5A and 5B), cucurbits (Crop Group 9), leafy vegetables, except *Brassica* (Crop Group 4), fruiting vegetables (Crop Group 8), hops, pome fruits (Crop Group 11), stone fruits (Crop Group 12), and tree nuts (Crop Group 14). Residue data from European residue trials in or on dry bulb onions, strawberries, and residue trials in the representative NAFTA growing regions in or on citrus (Crop Group 10) are sufficient to establish the import maximum residue limits.

No residues of spirotetramat, BYI08330-ketohydroxy, BYI08330-desmethyl-ketohydroxy, BYI08330-desmethyl-dihydroxy or BYI08330-ketohydroxy-alcohol were detected above the LOQ in rotational crops (mustard greens, turnips, wheat) at a plantback interval of 30 days. Therefore, a 30-day plantback interval restriction on the label is acceptable.

Residues of spirotetramat and the metabolites BYI 08330-enol, BYI 08330-ketohydroxy, BYI 08330-mono-hydroxy, and BYI 08330-enol-glucoside (Glc) concentrated in citrus oil (13.5-fold), apple pomace (1.9-fold), raisins (2.6-fold), prunes (2.2-fold), tomato paste (7.4-fold), tomato purée (3.5-fold), dried tomato (11.8-fold), potato flakes (3.5-fold) and potato chips (1.2-fold). However, separate MRLs will only be required for citrus oil, potato flakes and raisins.

The potential for secondary transfer of total spirotetramat residues to meat, milk and eggs exists because there are feedstuffs associated with the proposed uses on apples, citrus fruits, potatoes and almonds. The data from the cattle-feeding studies indicate that residues of spirotetramat and BYI08330-enol, expressed as BYI08330 equivalents, are expected at or below the limit of quantitation in meat and meat byproducts as a result of feeding livestock with crops treated with

spirotetramat. As none of the proposed target crops are considered a commodity for poultry feed, data depicting residues in laying hens are not required.

3.5.2 Dietary Risk Assessment

Chronic and acute dietary risk assessments were conducted using the Dietary Exposure Evaluation Model (DEEM–FCID™, Version 2.03).

3.5.2.1 Chronic Dietary Exposure Results and Characterization

A refined chronic dietary assessment was performed taking into account median residue trial data from treated crops, anticipated residues in animal commodities (meat, meat byproducts and milk), and experimental processing factors. The chronic dietary exposure estimates from all supported spirotetramat food uses range from 5.5% to 20% (0.0010993 mg/kg bw/day to 0.003991 mg/kg bw/day) of the ADI (0.02 mg/kg bw/day) for the total population, including infants and children. Aggregate exposure to spirotetramat from food and water is considered acceptable: 5.8% to 20.5% (0.001155 mg/kg bw/day to 0.004092 mg/kg bw/day) of the ADI for all representative population subgroups.

3.5.2.2 Acute Dietary Exposure Results and Characterization

A refined acute dietary assessment (deterministic, 95th percentile) was performed taking into account median residue trial data from treated crops, anticipated residues in animal commodities (meat, meat byproducts and milk) and experimental processing factors. Acute dietary exposure estimates from all supported spirotetramat food uses range from 0.3% to 1.1% (0.003211 mg/kg bw/day to 0.010749 mg/kg bw/day) of the ARfD (1 mg/kg bw/day) for the total population, including infants and children. Aggregate exposure to spirotetramat from food and water is considered acceptable: 0.4% to 1.1% (0.003444 mg/kg bw/day to 0.011314 mg/kg bw/day) of the ARfD for all representative population subgroups.

3.5.3 Aggregate Exposure and Risk

An aggregate risk assessment is required for people who enter treated orchards for "pick-your-own" activities. The aggregate risk for Movento 150 OD Insecticide or Movento 240 SC Insecticide consists of exposure from food and drinking water sources and dermal exposure from picking; there are no residential uses. Aggregate risks were calculated based on one-day dietary exposure from apples, chronic exposure from all dietary sources (food and water) and dermal exposure from picking treated apples. Dermal exposure to bystanders re-entering treated apple orchards is calculated by combining chemical-specific dislodgeable foliar residue (DFR) with activity-specific transfer coefficients. For the aggregate risk assessment, the NOAEL of 100 mg/kg bw from the rat acute neurotoxicity study was selected. Aggregate MOEs for adult and youth picking treated apples are above the target of 100 and are considered acceptable (Table 3.5.3.1)

Table 3.5.3.1 Aggregate Exposure for Both Adult and Youth Bystanders Performing Pick-Your-Own Activities in Apples

Population	U-pick Dermal	Acute Dietary	Chronic Dietary	Aggregate[1]	MOE (target 100)[2]
Apples (mg a.i./kg bw/day)					
Adults	0.005362	0.000170	0.001469	0.007	14284
Youths	0.009623	0.000353	0.001818	0.012	8479

[1] Aggregate exposure is the sum of dermal (from U-pick), acute dietary (commodity specific) and chronic dietary (from food and water) exposures.

[2] MOE = NOAEL/exposure, based on a NOAEL of 100 mg/kg bw from the rat acute neurotox study with a target of 100.

3.5.4 Proposed Maximum Residue Limits

Table 3.5.4.1 Proposed Maximum Residue Limits

Commodity	Recommended MRL (ppm)
For residues of spirotetramat and the metabolites BYI 08330-enol, BYI 08330-ketohydroxy, BYI 08330-mono-hydroxy and BYI 08330-enol-glucoside (Glc)	
Hops (dried)	10
Leafy Vegetables, except *Brassica,* Crop Group 4	9.0
Leafy *Brassica* Greens, Crop Subgroup 5B	8.0
Citrus oil	6.0
Stone Fruits, Crop Group 12	4.5
Raisins	3.0
Fruiting Vegetables, Crop Group 8	2.5
Head and Stem *Brassica*, Crop Subgroup 5A	2.5
Potatoe flakes	1.6
Small fruit vine climbing, except fuzzy kiwifruit, Crop Subgroup 13-07F	1.3
Pome Fruits, Crop Group 11	0.70
Citrus, Crop Group 10	0.60
Tuberous and Corm Vegetables, Crop Subgroup 1C	0.60
Strawberries	0.40
Cucurbit Vegetables, Crop Group 9	0.30
Dry Bulb Onions	0.30
Tree Nuts, Crop Group 14	0.25
For residues of spirotetramat and the metabolite BYI08330-enol	
Fat of cattle, goat, sheep and horse	0.02
Meat and meat byproducts of cattle, goat, sheep and horse	0.02
Milk	0.01

The nature of the residues in animal and plant matrices, analytical methodology, processing studies, field trial data and dietary risk estimates are summarized in Appendix I, Tables 1, 5 and 6.

4.0 Impact on the Environment

4.1 Fate and Behaviour in the Environment

Spirotetramat enters the terrestrial environment when it is used as an insecticide on a variety of crops, including fruits and vegetables. Biotransformation is the major route of transformation for spirotetramat in the terrestrial environment. Spirotetramat is non-persistent in soil and dissipates in less than a day under field and laboratory conditions. Major transformation products obtained from the biotransformation of spirotetramat in soil are spirotetramat-enol and spirotetramat-ketohydroxy. Under laboratory conditions, these transform with half-lives ranging from 3.3 to 12.3 days and 1.5 to 16.7 days, respectively. Phototransformation on soil is not expected to be a major route of transformation for spirotetramat. In a laboratory study, spirotetramat-enol, spirotetramat-ketohydroxy and dimethyl-benzoic acid were found to be major phototransformation products. Dimethyl-benzoic acid is a transformation product formed exclusively through phototransformation. This product is not expected to be found in important concentrations in the environment. In addition, the persistence of dimethyl-benzoic acid is not expected to be a concern based on the relatively simple structure of this compound. Spirotetramat is soluble in water and will not strongly bind to soil particles. Such characteristics typically increase the potential for leaching. However, because spirotetramat dissipates quickly, it is not expected that this compound will persist long enough to leach through the soil profile and enter groundwater. This is consistent with results of the drinking water modelling, which showed that spirotetramat does not leach to groundwater. Following a leaching assessment based on the groundwater ubiquity score (GUS), which takes into account the persistence and mobility of a compound, spirotetramat was classified as a non-leacher. In field studies, spirotetramat was not found below the soil surface layer (0–15 cm). Spirotetramat-enol and spirotetramat-ketohydroxy are more soluble and mobile than spirotetramat. Because of this, and because these products dissipate less quickly than spirotetramat, their potential for leaching is higher than for spirotetramat. Following a leaching assessment based on the GUS, these products were classified as borderline leachers. In laboratory soil column leaching studies, spirotetramat-enol was found only in the upper column layer but residues of spirotetramat-ketohydroxy were found throughout the column. In addition, spirotetramat-enol and spirotetramat-ketohydroxy were found in column leachates. Under field conditions, however, residues of spirotetramat-enol and spirotetramat-ketohydroxy were not found below 15 cm.

Spirotetramat could reach surface water systems by spray drift or runoff. Spirotetramat is non-persistent in water and will transform in approximately one day via biotransformation. In laboratory studies, spirotetramat-enol and spirotetramat-ketohydroxy were the major transformation products obtained from the aerobic biotransformation of spirotetramat in aquatic systems. Under aerobic conditions, spirotetramat-enol was more persistent than the parent (half-life ranging between 38 and 59 days) and spirotetramat-ketohydroxy was stable. Hydrolysis is unlikely to contribute to the dissipation of spirotetramat except under alkaline conditions. Spirotetramat hydrolyses into spirotetramat-enol, which has been shown to be stable to hydrolysis. Phototransformation may also contribute to the dissipation of spirotetramat under

alkaline conditions. Based on results from a phototransformation study performed in sterilized natural water (at pH 7.9), the net phototransformation half-life (corrected for hydrolysis) was 0.22 day, which is predicted to be approximately one day in Edmonton (Alberta). Major phototransformation products identified in this phototransformation study were spirotetramat-enol, methoxycyclohexanone and methoxycyclohexylaminocarboxylic acid.

Based on the vapour pressure and Henry's law constant, spirotetramat is considered to be non-volatile in the environment and is not expected to volatilize from water or moist soil surfaces. Therefore, residues of spirotetramat are not expected in the air and long-range transport is not expected.

Data on the fate and behaviour of spirotetramat, as well as the identification of its major transformation products, are summarized in Appendix I, Tables 7 and 8.

4.2 Effects on Non-Target Species

To estimate risk of potential adverse effects on non-target species, a deterministic quotient method is used. The risk quotient (RQ) is calculated by dividing the exposure estimate by an appropriate toxicity value. A screening level risk assessment is initially performed. For this assessment, conservative exposure estimates are used, such as those obtained from a direct application of the compound on soil or over a body of water. At the screening level, a risk quotient of less than one is considered to be below the level of concern (LOC) and no further assessment is necessary. If the screening level risk assessment results in a risk quotient above the level of concern of one, then refinements may be performed to further characterize the risk. A refined assessment takes into consideration more realistic exposure scenarios (such as drift to non-target habitats) and might consider different toxicity endpoints.

4.2.1 Effects on Terrestrial Organisms

Risk of spirotetramat, its related end-use products and transformation products to terrestrial organisms was based upon the evaluation of toxicity data for the following (Appendix I, Table 9):

- one earthworm species, one bee species, and four other arthropods representing invertebrates (acute and long-term exposure)
- two bird and two mammal species representing vertebrates (acute gavage, short- and long-term, reproduction, dietary exposure)
- ten crop species representing non-target vascular plants

4.2.1.1 Terrestrial Invertebrates

Spirotetramat and the spirotetramat-ketohydroxy transformation product were not acutely toxic to earthworms. In a chronic study, reproductive effects were observed for the spirotetramat-enol transformation product (a significant decrease in the number of juveniles was observed at higher doses). Risk quotients calculated at the screening level for earthworms did not exceed the level of concern (Appendix I, Table 10). Honeybees were not adversely affected by acute contact or oral exposure to spirotetramat and Movento 150 OD Insecticide under laboratory conditions.

Risk quotients calculated at the screening level for bees did not exceed the level of concern. However, semi-field tests using Movento 150 OD Insecticide have shown that this product affects the brood. A label statement is therefore included on the label to identify and mitigate the potential risk to honey bee broods. In other laboratory studies with beneficial arthropods, spirotetramat was found to be acutely toxic to two (*Aphidius rhopalosiphi* and *Typhlodromus pyri*) of the four species tested with Movento 150 OD Insecticide. Risk quotients calculated at the screening level exceeded the level of concern only for the predatory mite (*Typhlodromus pyri*) exposed to food contaminated with spirotetramat on the treated field (Apendix I, Table 10).

An off-field assessment was performed to better characterize the risk to beneficial arthropods (Appendix I, Table 12). This scenario assesses the risk to arthropods that may be exposed to spray drift in habitats adjacent to the treated field. For this assessment, the expected environmental concentration (EEC) off field was calculated based on the percent deposition one metre downwind according to the ground application model used at the PMRA. This model predicts the percent deposition at one metre to be 11% for applications using a groundboom sprayer and a fine spray quality, and 74% and 59% for airblast applications early in the season and late in the season, respectively. The off-field assessment showed that the level of concern was exceeded for the predatory mite (*Typhlodromus pyri*) in habitats adjacent to the treated field following airblast applications and applications using a groundboom sprayer. Therefore, appropriate label statements are included on the label to identify and mitigate the potential risk to some beneficial arthropods.

4.2.1.2 Terrestrial Vertebrates

Spirotetramat did not cause mortality in birds and small mammals in acute studies, although sublethal effects were observed in mallards at the lowest test concentration (diarrhea, soft excrement, reduced feed consumption). Also, there was no mortality in dietary studies with birds and mammals. Sublethal effects were observed in a 90-day dietary study with rats (such as adverse effects on the testes and spermatozoa). Observable reproductive effects were found in mallards (reduction in egg production, hatchability and offspring body weight) and bobwhite quail (reduction in mean hatchling body weight and reduction in the percent viable embryos/eggs set) and were also reported in a multigeneration reproduction study with rats (decrease in offspring body weight gain in males). Because exposure is dependent on the body weight of the organism and the amount and type of food consumed, the screening level risk assessment for birds and mammals considers a set of generic body weights (20, 100, 1000 g for birds and 15, 35, 1000 g for mammals) and food preferences (100% small insects for insectivores, 100% fruits for fructivores, 100% grain and seeds for granivores, and 100% leaves and leafy crops for herbivores; food items considered at the screening level present the most conservative EEC for each food guild). Additionally, the acute toxicity endpoint is divided by a factor of 10 to account for potential differences in species sensitivity as well as varying protection levels (e.g. community, population, individual). Risk quotients calculated at the screening level for birds and mammals exceeded the level of concern only for the reproduction of small and medium insectivorous birds, small fructivorous birds and large herbivorous birds exposed to food contaminated with spirotetramat on the treated field (Appendix I, Table 11).
Where the level of concern was exceeded, a refined assessment was performed to further characterize the risk to birds (Appendix I, Table 13). The risk associated with the consumption of food items contaminated from spray drift off the treated field was assessed. Also, additional

types of food items were considered for in-field and off-field assessments (for example, a diet consisting of large insects was considered for large and medium insectivorous birds and a diet consisting of vegetation other than leaves and leafy crops was considered for large herbivorous birds). Based on the refined assessment, the level of concern was not exceeded for ground applications but was exceeded in some cases of airblast application for small and medium insectivorous birds and for large herbivorous birds. Results of this assessment indicate that to reach the level of concern (risk quotient of one) for small and medium insectivorous birds, it would require that 69 to 88% of their diet be contaminated with spirotetramat. For large herbivorous birds, it would require that 49 to 61% (based on a diet of leaves and leafy crops) and 63 to 85% (based on short grass) of their diet be contaminated with spirotetramat to result in a risk quotient of one. This is considered to be a high proportion of a bird's diet, and consumption of such a high proportion of contaminated food items is unlikely to occur. Also, certain types of food items are less likely to be consumed in a large proportion (as would be the case for leaves and leafy crops). Additionally, while a number of conservative assumptions are made in the risk assessment, which maximize the estimated exposure levels, levels of spirotetramat are expected to decline relatively quickly under actual field conditions given its relatively short half-life (4.45 days on foliage). Therefore, the overall reproductive risk to birds is not expected to pose a concern.

4.2.1.3 Terrestrial Vascular Plants

For terrestrial plants, seedling emergence and vegetative vigour were examined. Only vegetative vigour was affected by Movento 150 OD Insecticide, with dry weight being the most sensitive endpoint. The vegetative vigour of two species (corn and ryegrass) was negatively affected by spirotetramat. Risk quotients calculated at the screening level exceeded the level of concern for corn (Appendix I, Table 10). A refined assessment characterized the risk to non-target plants off field (Appendix I, Table 12). The level of concern was exceeded, and therefore a ground buffer zone of one to two metres was calculated to protect sensitive non-target plant species in adjacent habitats.

4.2.2 Effects on Aquatic Organisms

Risk of spirotetramat, its related end-use products and transformation products to freshwater aquatic organisms was based upon the evaluation of toxicity data for the following (Appendix I, Table 9):

- two invertebrate species; daphnid and chironomid (acute and long-term exposure)
- five fish species (acute and long-term exposure)
- two green algae, one blue-green algae, one diatom and one vascular plant
- amphibian species using fish as surrogate

Risk of spirotetramat to marine aquatic organisms was based upon evaluation of toxicity data for the following (Appendix I, Table 9):

- two invertebrates; mysid and eastern oyster (acute exposure)
- one fish species (acute exposure)
- one diatom

4.2.2.1 Aquatic Invertebrates

Acute exposures to spirotetramat did not cause immobilization or sublethal effects in daphnids but had an adverse effect on other tested invertebrate species (resulted in mortality in chironomids and mysid shrimp, and inhibited shell growth of eastern oysters). In limit tests, the effect of transformation products on aquatic invertebrates varied. Spirotetramat-enol did not affect daphnids but affected chironomids; spirotetramat-ketohydroxy and methoxycyclohexylaminocarboxylic resulted in no adverse effects in chironomids (daphnids were not tested with this product); and methoxycyclohexanone resulted in no adverse effects in daphnids and chironomids. In long-term studies, spirotetramat had adverse effects on the reproduction of daphnids (decrease in the number of offspring per surviving parent) and chironomids (delayed effect in both emergence and development). At the screening level, the risk quotients were calculated using the estimated environmental concentration (EEC) in an 80-cm deep water body. Also, the acute toxicity value was divided by two to account for differences in species sensitivity as well as varying protection goals (e.g. community, population, individual). The risk quotients calculated at the screening level for invertebrates did not exceed the level of concern (Appendix I, Table 10).

4.2.2.2 Fish

In acute tests with freshwater and saltwater fish, mortality was observed following exposures to spirotetramat. In limit tests, no mortality occurred in freshwater fish following an exposure to spirotetramat-enol and methoxycyclohexanone. In an early life stage toxicity test with the fathead minnow, spirotetramat had an adverse effect on hatchability, fry survival and growth. Risk quotients calculated at the screening level for fish (using the EEC in an 80-cm deep water body and dividing the acute toxicity value by 10 to account for differences in species sensitivity as well as varying protection goals) did not exceed the level of concern (Appendix I, Table 10).

4.2.2.3 Algae and Aquatic Vascular Plants

The biomass and growth rate of green algae, blue-green algae and diatoms (both freshwater and saltwater species) were adversely affected by spirotetramat, with biomass being the most sensitive endpoint for these organisms. Spirotetramat-enol and methoxycyclohexanone did not have an adverse effect on green algae. The yield and growth rate of vascular plants were affected by spirotetramat and spirotetramat-enol, with yield being the most sensitive endpoint. Risk quotients calculated at the screening level for algae and aquatic vascular plants (using the EEC in an 80-cm deep water body and dividing the acute toxicity value by two to account for differences in species sensitivity as well as varying protection goals) did not exceed the level of concern (Appendix I, Table 10).

4.2.2.4 Amphibians

To assess the risk to amphibians for acute and chronic exposure, the toxicity values for the most sensitive fish species were used as surrogate data along with the EEC in a 15-cm deep body of water (this water depth is representative of a seasonal water body used by amphibians to reproduce). The risk quotients calculated at the screening level did not exceed the level of concern for amphibians (Appendix I, Table 10).

5.0 Value

5.1 Effectiveness Against Pests

5.1.1 Acceptable Efficacy Claims

Data from efficacy studies conducted between 2003 and 2004 in the United States (e.g. Florida, California, Oregon, Washington, New Jersey and New York) were submitted. Where multiple pests were present in one study, each pest species was considered as one trial for the purposes of summary by pest. Therefore, 59 trials were reviewed. For most trials, an appropriate experimental design was employed, which included an untreated control as well as a positive control. The control of individual insect species or the reduction in damage caused by insect pests was assessed visually and compared to an untreated control. Observations were made at various times throughout the growing season after treatment(s) occurred.

5.1.1.1 Foliar Applications of Movento 150 OD Insecticide and Movento 240 SC Insecticide

The submitted efficacy data established acceptable rates for all pests. Pest biology and efficacy are expected to be similar on all the listed crops within a crop group; therefore, data were extrapolated to all crops within a group. Where the label recommended control of the same pest on a variety of crops (e.g. whiteflies on cucurbits and fruiting vegetables), the data demonstrated that different rates were not required; therefore, the crops were grouped (e.g. field vegetables) and the rate for a particular pest was standardized. The accepted rates are identified in Section 1.3, Table 1.3.1.

5.2 Phytotoxicity to Host Plants

Phytotoxicity observations were made and recorded in most of the 59 efficacy trials conducted in 2003 and 2004. Four additional trials were conducted in 2005, specifically to observe the non-safety adverse effects on pome fruits.

5.2.1 Acceptable Claims for Host Plants

Phytotoxicity was observed in only five efficacy trials (two on apple, two on pear and one on pepper). The injuries were mainly bronzing, minor leaf margin burning and necrotic spotting of leaves and fruits. Specific causes of injury observed in these trials were attributed to a) overspray (i.e. trial errors), b) high temperatures and/or c) the use of an adjuvant. Therefore, all crops in the following crop groups are acceptable: grapes (excluding table grapes) and small fruit vine crops, pome fruits, stone fruits, tree nuts, hops, cucurbits, fruiting vegetables, leafy vegetables–both *Brassica* and non-*Brassica*–and tuberous and corm vegetables.

5.3 Impact on Succeeding Crops

The impact on succeeding crops was not evaluated in this product review.

5.3.1 Acceptable Claims for Rotational Crops

Rotational crops were not assessed in this product review.

5.4 Economics

No market analysis was assessed for this product review.

5.5 Sustainability

5.5.1 Survey of Alternatives

Alternative active ingredients vary depending on the pest. Many of the currently available alternatives are older classes of insecticides, such as carbamates, organophosphates and organochlorines. Other alternatives include the classes synthetic pyrethroids and neonicotinoids as well as protectant kaolin clay. The major alternatives currently registered for control of pests on apple, peach, grape, tree nuts, cucumber, tomato, lettuce, cabbage and potato are listed in Appendix I, Table 14.

Spirotetramat is believed to be a member of the lipid synthesis inhibitor class of insecticides. Products containing active ingredients in this group are currently registered in Canada. These include Forbid 240 SC (spiromesifen) to control whiteflies and several species of mites on field and greenhouse ornamentals, greenhouse vegetables, corn, strawberries and a variety of other vegetables, and Envidor 240 SC Miticide (spirodiclofen) to control mites on pome and stone fruit and grapes. For pests currently not listed on any Group 23 insecticide labels, spirotetramat could provide a new active ingredient with which to alternate for the prevention of resistance.

5.5.2 Compatibility with Current Management Practices Including Integrated Pest Management

Movento 150 OD Insecticide and Movento 240 SC Insecticide offer relatively specific insect control when used in tree fruit and vegetable crops. They are also compatible with current management practices and conventional crop production systems. Where thresholds exist, users are familiar with monitoring techniques to determine if and when applications are needed.

The effect of spirotetramat on commonly occurring predators and parasitoids of orchards and field vegetables was not assessed from a value perspective. Based on the environmental review, spirotetramat may pose a risk to some beneficial arthropods. Therefore, no claim regarding the acceptability of Movento 150 OD Insecticide and Movento 240 SC Insecticide in an integrated pest management system can be made.

5.5.3 Information on the Occurrence or Possible Occurrence of the Development of Resistance

Repeated use of insecticides with the same mode of action increases the probability of naturally selecting resistant biotypes within an insect population. Therefore, Movento 150 OD Insecticide

and Movento 240 SC Insecticide should be used in rotation with insecticides that have different modes of action.

The Movento 150 OD Insecticide and Movento 240 SC Insecticide labels include the resistance management statements, as per Regulatory Directive DIR99-06, *Voluntary Pesticide Resistance-Management Labelling Based on Target Site/Mode of Action*.

5.5.4 Contribution to Risk Reduction and Sustainability

Spirotetramat controls a broader range of pests compared to currently registered lipid biosynthesis inhibitors. As well, spirotetramat can be used on a wider range of crops. Spirotetramat is the first group 23 insecticide registered for control of mealybugs, phylloxera, pear psylla, aphids, and scale. For these pests, spirotetramat is a new active ingredient with which to rotate for resistance management. Prudent use of insecticides in this class should be observed to prevent the development of resistance because spiromesifen and spirodiclofen are already registered for use on several of the labeled crops. Several of the pests on the Movento 150 OD Insecticide and Movento 240 SC Insecticide labels are controlled by older chemistries such as organophosphates. As such, spirotetramat is considered to be an organophosphate replacement.

6.0 Toxic Substances Management Policy Considerations

The management of toxic substances is guided by the federal government's Toxic Substances Management Policy, which puts forward a preventive and precautionary approach to deal with substances that enter the environment and could harm the environment or human health. The policy provides decision makers with direction and sets out a science-based management framework to ensure that federal programs are consistent with its objectives. One of the key management objectives is virtual elimination from the environment of toxic substances that result predominantly from human activity and that are persistent and bioaccumulative. These substances are referred to in the policy as Track 1 substances.

During the review process, spirotetramat was assessed in accordance with the PMRA Regulatory Directive DIR99-03, *The Pest Management Regulatory Agency's Strategy for Implementing the Toxic Substances Management Policy*. Substances associated with the use of spirotetramat were also considered, including major transformation products formed in the environment, microcontaminants in the technical product and formulants in the end-use products, Movento 150 OD Insecticide and Movento 240 SC Insecticide. The PMRA has reached the following conclusions:

- Spirotetramat does not meet the criteria for persistence, as its values for half-life in water (1.05–1.06 days) and soil (0.10–0.38 days) are below the TSMP Track 1 cut-off criteria for water (≥182 days) and soil (≥182 days). The vapour pressure (5.6×10^{-9} Pa or 4.2×10^{-11} mmHg at 20°C) and Henry's law constant (6.9×10^{-13} atm m^3/mole) for spirotetramat indicate that volatilization is not an important route of dissipation, and therefore long-range atmospheric transport is not likely to occur. Spirotetramat is not bioaccumulative, with an octanol–water partition coefficient (log K_{ow}) of 2.5, which is below the TSMP Track 1 cut-off criterion of ≥5.0.

- Spirotetramat-enol and spirotetramat-ketohydroxy, which are major transformation products of spirotetramat, do not meet the TSMP Track 1 criteria. The half-life of spirotetramat-enol was found to be 37.9–59.0 and 3.3–12.3 days in water and soil, respectively. The half-life of spirotetramat-ketohydroxy in soil is 1.5–16.7 days. These values are below the TSMP Track 1 cut-off criteria for water (≥182 days) and soil (≥182 days). Also, spirotetramat-enol and spirotetramat-ketohydroxy are not bioaccumulative, with a an octanol–water partition coefficient (log K_{ow}) of up to 2.0 and 1.3, respectively, which is below the TSMP Track 1 cut-off criterion of ≥5.0.

- Technical grade spirotetramat does not contain any contaminants of health or environmental concern identified in the *Canada Gazette*, Part II, Volume 139, Number 24, pages 2641–2643: *List of Pest Control Product Formulants and Contaminants of Health or Environmental Concern*.

- The end-use products Movento 150 OD Insecticide and Movento 240 SC Insecticide do not contain any formulants of health or environmental concern identified in the *Canada Gazette*, Part II, Volume 139, Number 24, pages 2641–2643: *List of Pest Control Product Formulants and Contaminants of Health or Environmental Concern*.

Therefore, the use of spirotetramat is not expected to result in the entry of Track 1 substances into the environment.

7.0 Summary

7.1 Human Health and Safety

The toxicology database submitted for spirotetramat is adequate to define the majority of toxic effects that may result from human exposure to spirotetramat. Spirotetramat was not carcinogenic or genotoxic. Spirotetramat was not teratogenic in rabbits and was teratogenic in rats only at maternally toxic doses. There was variability in toxicological response among test species, which may reflect differences in metabolism. Mice were relatively insensitive to the test substance whereas adverse effects were observed in the rat and the dog. In the rat, males appeared to be more sensitive to spirotetramat toxicity than females, with the male reproductive system (sperm, testes and epididymides) identified as a target for toxicity. Sperm toxicity was noted in F_1 males at lower doses than in the P-generation males. The most sensitive test species appeared to be the dog, as evidenced by thymus and central nervous system effects as well as perturbations in thyroid hormones. There was evidence of clinical signs of neurotoxicity as well as brain pathology in the dog. The implications of the thyroid and brain findings in adult dogs as they relate to neuroendocrine development of the young animal were taken into account in the risk assessment.

The nature of the residue in plants and ruminants is adequately understood. The proposed uses of spirotetramat in or on tuberous and corm vegetables, grapes and small fruit vine climbing, *Brassica* leafy vegetables, cucurbit vegetables leafy vegetables (except *Brassica*), fruiting vegetables, hops (dried), pome fruits, stone fruits, tree nuts, imported dry bulb onions, citrus and strawberries do not constitute an unacceptable chronic or acute dietary risk (food and drinking water) to any segment of the population, including infants, children, adults and seniors.

Sufficient crop residue data have been reviewed to recommend maximum residue limits to protect human health (Table 3.5.4.1).

Mixers, loaders and applicators handling Movento 150 OD Insecticide or Movento 240 SC Insecticide and workers re-entering treated fields are not expected to be exposed to levels of spirotetramat that will result in unacceptable risk when the product is used according to label directions.

A health assessment has been conducted, and Movento 150 OD Insecticide or Movento 240 SC Insecticide use on vegetables, pome and stone fruit, grapes, tree nuts and hops is not expected to result in unacceptable risk.

7.2 Environmental Risk

The use of Movento 150 OD Insecticide and Movento 240 SC Insecticide may pose a risk to terrestrial organisms, including bees, beneficial arthropods and terrestrial non-target vascular plants. Precautionary label statements appear on the product labels to identify and mitigate this risk. Also, buffer zones of one to two metres are required to protect sensitive non-target plant species from spray drift. While spirotetramat is toxic to certain aquatic organisms, it is not expected that the use of Movento 150 OD Insecticide and Movento 240 SC Insecticide will pose a risk to aquatic organisms when used according to label directions.

7.3 Value

The data submitted to register Movento 150 OD Insecticide and Movento 240 SC Insecticide are adequate to describe its efficacy for use in a variety of tree fruit and vegetable crops. Movento 150 OD Insecticide and Movento 240 SC Insecticide offer control or suppression of a variety of insect pests when applied according to the directions for use identified on the label.

7.4 Unsupported Uses

Certain uses originally proposed by the applicant were not supported by the PMRA because the value was not adequately demonstrated. These uses include: 1) pests—mites, micro-lepidoptera leafminers, white apple leafhopper, black scale, cherry fruit fly, diamond back moth, potato tuberworm and olive scale; 2) crops—Christmas trees; and 3) application methods—chemigation and aerial. See Appendix I, Table 15.

8.0 Proposed Regulatory Decision

Health Canada's PMRA, under the authority of the *Pest Control Products Act*, is proposing full registration for the sale and use of Spirotetramat Technical Insecticide, Movento 150 OD Insecticide and Movento 240 SC Insecticide containing the technical grade active ingredient spirotetramat to control a variety of insect pests on the labelled field vegetable crops, tree fruits, hops, and grapes (excluding table grapes) and small fruit vine crops. An evaluation of available scientific information found that, under the proposed conditions of use, the products have value and do not present an unacceptable risk to human health or the environment.

List of Abbreviations

a.i.	active ingredient
ADI	acceptable daily intake
ALS	acetolactate synthase
AR	applied radioactivity
ARfD	acute reference dose
atm	atmosphere
bw	body weight
CAS	Chemical Abstracts Service
cm	centimetre(s)
d	day(s)
DNA	deoxyribonucleic acid
DT_{50}	dissipation time 50% (dose required to observe a 50% decline of test population)
DT_{75}	dissipation time 75% (dose required to observe a 75% decline of test population)
DT_{90}	dissipation time 90% (dose required to observe a 90% decline of test population)
EC_{10}	effective concentration on 10% of the population
EC_{25}	effective concentration on 25% of the population
EC_{50}	effective concentration on 50% of the population
EEC	estimated environmental concentration
ELS	early life stages
ER_{25}	effective rate for 25% of the population
FIR	food ingestion rate
g	gram(s)
GLP	Good Laboratory Practice
GUS	groundwater ubiquity score
h	hour(s)
ha	hectare(s)
HAFT	highest average field trial
Hg	mercury
HPLC	high performance liquid chromatography
IUPAC	International Union of Pure and Applied Chemistry
kBq	kilo Becquerel
kg	kilogram(s)
K_d	soil-water partition coefficient
km	kilometre(s)
K_{oc}	organic carbon partition coefficient
K_{ow}	*n*-octanol–water partition coefficient
L	litre(s)
LC_{50}	lethal concentration 50%
LD_{50}	lethal dose 50%
LLNA	local lymph node assay
LOAEL	lowest observed adverse effect level
LOC	level of concern
LOD	level of detection
LOQ	limit of quantitation
LR_{50}	lethal rate 50%

m/z	mass to charge ratio
mg	milligram
mL	millilitre(s)
mm	millimetre(s)
MAS	maximum average score
MOE	margin of exposure
MRL	maximum residue limit
MRM	multiple reaction monitoring
MS	mass spectrometry
N/A	not applicable
NAFTA	North American Free Trade Agreement
NOAEL	no observed adverse effect level
NOEC	no observed effect concentration
NOEL	no observed effect level
NZW	New Zealand White
OC	organic carbon content
OD	oil dispersible
OECD	Organisation for Economic Co-operation and Development
OM	organic matter content
PBI	plantback interval
PHI	preharvest interval
pK_a	dissociation constant
PMRA	Pest Management Regulatory Agency
ppb	parts per billion
ppm	parts per million
RAC	raw agricultural commodity
RQ	risk quotient
SC	soluble concentrate
$t_{1/2}$	half-life
T_3	tri-iodothyronine
T_4	thyroxine
TRR	total radioactive residue
TSMP	Toxic Substances Management Policy
UF	uncertainty factor
USEPA	United States Environmental Protection Agency
UV	ultraviolet
v/v	volume per volume dilution
µg	microgram(s)
µL	microlitre(s)
wk	week(s)
yr	year(s)

Appendix I Tables and Figures

Table 1 Residue Analysis

Method ID	Analyte	Method Type	LOQ		Reference
Plant Matrices					
00857 00857/E001 00857/M003 01084	BYI 08330 BYI 08330-enol BYI 08330-ketohydroxy BYI 08330-mono-hydroxy BYI 08330-enol-glucoside	Data gathering and enforcement: HPLC-ESI-MS/MS	0.01 ppm for each analyte	Potato (Crop Subgroup 1C), grape, Brassica vegetable (Crop Groups 5A and 5B), cucurbit (Crop Group 9), leafy vegetable, except Brassica (Crop Group 4), citrus (Crop Group 10), fruiting vegetable (Crop Group 8), hop, pome fruit (Crop Group 11), stone fruit (Crop Group 12), tree nut (Crop Group 14), bulb onion (Crop Group 3A) and strawberry	1314310 1314689 1314624 1314682 1565993
			0.1 ppm for each analyte	Hops cones	
1st MRM*: BYI 08330 374 to 216 m/z; BYI 08330-enol 302 to 216 m/z; BYI 08330-ketohydroxy 318 to 268 m/z; BYI 08330-mono-hydroxy 304 to 254 m/z; BYI 08330-enol-Glc 464 to 270 m/z. 2nd MRM (for confirmation): BYI 08330 374 to 302 m/z; BYI 08330-enol 302 to 270 m/z; BYI 08330-ketohydroxy 318 to 214 m/z; BYI 08330-mono-hydroxy 304 to 119 m/z; BYI 08330-enol-Glc 464 to 216 m/z.					
00929	BYI 08330-ketohydroxy-alcohol, BYI 08330-desmethyl-ketohydroxy, and BYI 08330-desmethyl-di-hydroxy	Data gathering: HPLC-ESI-MS/MS	0.02 ppm for each analyte	Rotational crops: wheat (grain, forage, straw and flour), cotton undelinted seeds, Swiss chard, peanut (oil and nutmeat), and sugar beets (roots and molasses)	1314377 1314696
BYI 08330-ketohydroxy-alcohol 334 to 298 m/z; BYI 08330-desmethyl-ketohydroxy 304 to 268 m/z; BYI 08330-desmethyl-di-hydroxy 306 to 227 m/z.					
Animal Matrices					
00966	BYI 08330, BYI 08330-enol, BYI 08330-enol-glucuronide	Data gathering: HPLC-ESI-MS/MS	0.005 ppm for each analyte	Milk	1314326 1314614 1314664
			0.01 ppm for each analyte	Fat, liver, kidney, muscle, egg	
00969	BYI 08330, BYI 08330-enol	Enforcement: HPLC-ESI-MS/MS	0.005 ppm	Milk	1314401 1314486 1314229
			0.01 ppm	Fat, liver, kidney, muscle, egg	
1st MRM: BYI 08330 374 to 216 m/z; BYI 08330-enol 302 to 216 m/z; BYI 08330-enol-GA 478 to 302 m/z. 2nd MRM (for confirmation): BYI 08330 374 to 302 m/z; BYI 08330-enol 302 to 270 m/z; BYI 08330-enol-GA 478 to 216 m/z.					

Method ID	Analyte	Method Type	LOQ		Reference
Soil and Sediment Matrices					
00986	Active (BYI08330)	HPLC/MS/MS m/z 302 and 216	5 ppb	The analytical method provided for the soil samples is also used for sediment.	1314201
	BYI08330-enol	HPLC/MS/MS m/z 270 and 216			
Water Matrix					
00836	Active (BYI08330)	HPLC/MS/MS m/z 302 and 216	0.05 ppb		1314562
	BYI08330-enol	HPLC/MS/MS m/z 270 and 216			

* MRM – Multiple reaction monitoring

Table 2 Acute Toxicity of Spirotetramat and Its Associated End-Use Products (Movento 150 OD Insecticide and Movento 240 SC Insecticide)

Study Type	Species	Result	Comment	Reference
Acute Toxicity of Spirotetramat Technical				
Oral (up and down)	Rat	LD_{50} > 2000 mg/kg bw	Low toxicity	1314092
Dermal	Rat	LD_{50} > 2000 mg/kg bw	Low toxicity	1314228
Inhalation	Rat	LC_{50} > 4.183 mg/L	Low toxicity	1314557
Skin irritation	Rabbit	MAS/MIS = 0	Non-irritating	1314213
Eye irritation	Rabbit	MAS = 26 Unable to calculate MIS due to lack of values for 1 h	Moderately irritating	1314211
Skin sensitization (maximization)	Guinea pig	Positive	Dermal sensitizer	1314185
Skin sensitization (Buehler)	Guinea pig	Negative	Not a dermal sensitizer	1314216
Skin sensitization (LLNA)	Mouse	Stimulation Index = 3.2 – 5.9 Positive	Dermal sensitizer	1314294
Oral (Acute Toxic Class) BYI 08330-CIS-Ketohydroxy metabolite	Rat	LD_{50} > 2000 mg/kg bw	Low toxicity	1314283
Oral (Acute Toxic Class) BYI 08330-desmethyl-ketohydroxy metabolite	Rat	LD_{50} > 2000 mg/kg bw	Low toxicity	1314285

Study Type	Species	Result	Comment	Reference
Oral (Acute Toxic Class) BYI 08330-di-hydroxy metabolite	Rat	LD_{50} > 2000 mg/kg bw	Low toxicity	1314427
Oral (Acute Toxic Class) BYI 08330-mono-hydroxy metabolite	Rat	LD_{50} > 2000 mg/kg bw	Low toxicity	1314474
Acute Toxicity of End-Use Product – Movento 150 OD Insecticide				
Oral (Acute Toxic Class)	Rat	LD_{50} > 2000 mg/kg bw	Low toxicity	1314219
Dermal	Rat	LD_{50} > 4000 mg/kg bw	Low toxicity	1314221
Inhalation	Rat	LC_{50} > 1.76 mg/L	Slightly toxic	1314282
Skin irritation	Rabbit	MAS = 1.4 MIS = 1.7	Slightly irritating	1314161
Eye irritation	Rabbit	MAS = 32 MIS = 42.7	Severely irritating Corneal opacity and conjunctival irritation, redness and chemosis not resolved until day 21.	1314212
Skin sensitization (Buehler)	Guinea pig	Positive	Dermal sensitizer	1314218
Skin sensitization with 0.48% test material (Buehler)	Guinean pig	Negative	Not a dermal sensitizer	1314284
Acute Toxicity of End-Use Product – Movento 240 SC Insecticide				
Oral (Acute Toxic Class)	Rat	LD_{50} > 2000 mg/kg bw	Low toxicity	1314220
Dermal	Rat	LD_{50} > 4000 mg/kg bw	Low toxicity	1314222
Inhalation	Rat	LC_{50} > 3.013 mg/L	Low toxicity	1314297
Skin irritation	Rabbit	MAS/MIS = 0	Non-irritating	1314278
Eye irritation	Rabbit	MAS = 0.67 MIS = 2	Minimally irritating	1314223
Skin sensitization (Buehler)	Guinea pig	Positive	Dermal sensitizer	1314281
Skin sensitization with 0.3% test material (Buehler)	Guinea pig	Negative	Not a dermal sensitizer	1314296

MAS = maximum average score for 24, 28 and 72 hours
MIS = maximum irritation score

Table 3 Toxicity Profile of Technical Spirotetramat

Study Type	Species	Results[1] (mg/kg bw/day in males/females)	Reference
4-week dietary range-finding	Rat	Effect levels not established since study considered supplemental. No compound-related effects were observed on measured parameters.	1314554
4-week dietary range-finding	Mouse	Effect levels not established since study considered supplemental. No compound-related effects were observed on measured parameters.	1314584
28-day dermal	Rat	Systemic toxicity: NOAEL: 1000 mg/kg bw/day LOAEL: Not established Dermal irritation: NOAEL: 1000 mg/kg bw/day LOAEL: Not established	1314466
90-day dietary	Rat	NOAEL: 148/188 mg/kg bw/day LOAEL: 616/752 mg/kg bw/day, based on ↓ body weight gain (♂), ↓ absolute kidney wt (♂), ↓ absolute testis weight, abnormal spermatozoa and hypospermia noted in epididymis, tubular degeneration, vacuolization of the testes, increased incidence of alveolar macrophages in the lung.	1314138
90-day dietary	Mouse	NOAEL: 1305/1515 mg/kg bw/day LOAEL: Not established	1314367
28-day dietary	Dog	Effect levels were not established since this study was considered supplemental (only 2 dogs/sex/dose group). The following effects were noted at a dose level of 104/127 mg/kg bw/day: emaciation and thinness in 1 ♂ and 2 ♀,mild hind-limb wheelbarrowing deficit in 1 ♀, muscular atrophy associated with reduced postural reactions in the other ♀ and 1 ♂, ↓ body weight, body weight loss, ↓ food consumption, ↓ T_4, T_3 & TSH (♀), ↓ calcium and albumin, ↓ thymus size, ↓ absolute/relative thymus weight, exacerbated sexual immaturity in 1 ♂ (animal also had mild diffuse atrophy of parotid salivary glands), thymic involution in 1 ♂ and 2 ♀.	1314139
90-day dietary	Dog	NOAEL(♂): 81 mg/kg bw/day LOAEL(♂): Not established NOAEL(♀): 32 mg/kg bw/day LOAEL(♀): 72 mg/kg bw/day, based on clinical signs of toxicity in 1 ♀ (thin, abnormal posture, reluctant to stand) ↓ body weight gain and food consumption, ↓ rbc, hemoglobin and hematocrit, thymus atrophy (1♀), ↓ T_3 and T_4	1314154

Study Type	Species	Results[1] (mg/kg bw/day in males/females)	Reference
1-year dietary	Dog	NOAEL: 6/5 mg/kg bw/day LOAEL: 20/19 mg/kg bw/day, based on ↓ thymus size (involution; mild) (1 ♂), dilation of brain ventricle (cerebrum) in 1 ♂ (mild) and 1 ♀ (moderate), ↓ T_4	1314428
1-year dietary 10 rats/sex/dose assessed for neurotoxicity (FOB) during the 12th month of the study.	Rat	NOAEL: 13.2 mg/kg bw/day LOAEL: 189 mg/kg bw/day, based on ↑ incidence of minimal to slight accumulation of alveolar macrophages in males	1314245
Chronic/ carcinogenicity (2-year dietary)	Rat	NOAEL: 12.5/16.8 mg/kg bw/day LOAEL: 169/229 mg/kg bw/day, based on ↓ absolute kidney weight, ↑ incidence of renal tubular dilatation.	1314327
Carcinogenicity (18-month dietary)	Mouse	NOAEL: 1022/1319 mg/kg bw/day LOAEL: Not established	1314721
One-generation reproduction (range-finding)	Rat	Effect levels not established since this was a range-finding study. Parental (↓ body weight gain in females during premating and lactation) and offspring (↓ body weight and body weight gain during lactation) systemic effects noted at 320/384 mg/kg bw/day Reproductive effects noted in F_1 8-9 wk old males at 320 mg/kg bw/day and in P-gen males at 538 mg/kg bw/day: ↓ sperm motility and progression, ↑ abnormal sperm cells (amorphous sperm heads), ↓ cauda epididymis weight (P-gen only) Lack of pregnancies and absence of implantation sites in dams at 538/646 mg/kg bw/day	1314555

Study Type	Species	Results[1] (mg/kg bw/day in males/females)	Reference
Two-generation reproduction	Rat	Parental toxicity: NOAEL: 71/83 mg/kg bw/day LOAEL: 419/485 mg/kg bw/day Based on ↓ body weight during pre-mating, gestation and lactation, ↓ body weight gain during pre-mating and gestation, ↓ food consumption during lactation, kidney histopathology (tubular dilatation), and ↓ absolute and relative kidney weights Offspring toxicity: NOAEL: 17/20 mg/kg bw/day LOAEL: 71/83 mg/kg bw/day, based on ↓ bwg in F_2 during lactation interval day 14-21 (♂) (corresponds to the time frame when pups are beginning to consume diet and are therefore receiving a higher intake on a mg/kg bw basis) Reproductive toxicity: Males NOAEL: 71 mg/kg bw/day LOAEL: 419 mg/kg bw/day, based on ↑ abnormal sperm cells (amorphous sperm heads) in F_1 and ↓ fertility in one F_1 male Females NOAEL: 485 mg/kg bw/day LOAEL: Not established	1314542
Developmental toxicity (range-finding)	Rabbit	Effect levels not established since this was a range-finding study (study report was limited to a 2-page executive summary; only 3 inseminated females/dose level). Maternal toxicity (cold ears, ↓ food consumption and body weight loss) noted at 160 mg/kg bw/day. Developmental toxicity (single malformation; cardiac ventricular septal defect) noted at 25 mg/kg bw/day.	1314563
Developmental toxicity	Rabbit	Maternal: NOAEL: 10 mg/kg bw/day LOAEL: 40 mg/kg bw/day, based on one dam that aborted on gestation day 24 (dam also exhibited severe body weight loss, ↓ food consumption, ↓ urination and discoloured urine). Developmental: NOAEL: 160 mg/kg bw/day LOAEL: Not established No indication of developmental toxicity at the highest dose tested.	1314225

Study Type	Species	Results[1] (mg/kg bw/day in males/females)	Reference
Developmental toxicity (range-finding)	Rat	Effect levels not established since this was a range-finding study (study report was limited to a 2-page executive summary). Maternal toxicity (↓ body weight and body weight gain) at 800 mg/kg bw/day. Developmental toxicity at 200 mg/kg bw/day (↓ fetal weight, dysplastic tubular bones in 1 fetus).	1314438
Developmental toxicity	Rat	Maternal: NOAEL: 140 mg/kg bw/day LOAEL: 1000 mg/kg bw/day, based on ↓ food consumption, ↓ body weight and body weight gain Developmental: NOAEL: 140 mg/kg bw/day LOAEL: 1000 mg/kg bw/day, based on the following malformations: cleft palate (1 fetus), co-arctation of aortic arch between left carotid and left subclavian arteries, ascending aorta reduced in size and left subclavian artery arises from descending aorta (1 fetus), dysplasia of forelimb bones, altered appearance of sacral vertebral arch with pelvic shift, supernumerary lumbar vertebra (1 fetus). Increased incidence of numerous skeletal variations and ↓ body weight also observed at this dose. Teratogenic at maternally toxic doses.	1314272
Developmental toxicity (Study conducted to further investigate possible treatment-related effects in the developmental study at doses ≤140 mg/kg bw/day)	Rat	Maternal: NOAEL: 140 mg/kg bw/day LOAEL: Not established Developmental: NOAEL: 140 mg/kg bw/day LOAEL: Not established	1314279
Reverse gene mutation assay in bacteria	Salmonella typhimurium strains TA 98, TA 100, TA 102, TA 1535, TA 1537	Negative	1314217
Reverse gene mutation assay in bacteria	Salmonella typhimurium strains TA 98, TA 100, TA 102, TA 1535, TA 1537	Negative	1314331
Gene mutations in mammalian cells in vitro	Chinese hamster V79 cells (HGPRT locus)	Negative	1314382

Study Type	Species	Results[1] (mg/kg bw/day in males/females)	Reference
In vivo unscheduled DNA synthesis	Primary rat hepatocytes from male rats	Negative	1314215
In vitro mammalian chromosomal aberration	Chinese hamster V79 cells	Positive	1314341
In vitro mammalian chromosomal aberration	Chinese hamster V79 cells	Negative *Unacceptable, non-guideline (only one dose group, no positive control, non-GLP)	1314318
In vivo mammalian chromosomal aberration	NMRI male mice	Negative	1314162
In vivo micronucleus assay	NMRI male mice	Negative	1314214
Genotoxicity of metabolites			
Reverse gene mutation assay in bacteria BYI 08330 mono-hydroxy	Salmonella typhimurium strains TA 98, TA 100, TA 102, TA 1535, TA 1537	Negative	1314160
Reverse gene mutation assay in bacteria BYI 08330 di-hydroxy	Salmonella typhimurium strains TA 98, TA 100, TA 102, TA 1535, TA 1537	Negative	1314330
Reverse gene mutation assay in bacteria BYI 08330 desmethyl-ketohydroxy	Salmonella typhimurium strains TA 98, TA 100, TA 102, TA 1535, TA 1537	Negative	1314329
Special Studies			
Acute neurotoxicity	Rat	NOAEL: 100 mg/kg bw LOAEL: 200 mg/kg bw, based on clinical signs (urine stain), ↓ locomotor activity and ↓ interval locomotor activity on day 0	1314156
10-day oral range-finding with BYI 08330-enol metabolite 800 mg/kg bw/day	Rat	Effect levels not established since this study was considered supplemental (only one dose level, limited parameters examined). No treatment-related effects on survival, no clinical signs of toxicity. Food consumption was 19% lower on day 10 than on day 7. Treated rats showed a lack of body weight gain (mean of 1 g).	1314560

Study Type	Species	Results[1] (mg/kg bw/day in males/females)	Reference
Reproductive toxicity in males: identification of primary target cell in testis and epididymis Oral gavage at 1000 mg/kg bw/day and sacrificed after 3, 10, 21 or 41 days of treatment	Rat	Effects levels not established One animal died on day 31 (cause of death undetermined). Increased salivation and reduced bwg prior to death. Localized soiled fur observed in all animals. Clinical signs observed in one or two animals. Each included reduced motor activity, tremors, hunched posture, skin lesions. ↓ food consumption during 1st week, bw loss during 1st week, ↓ bwg for remainder of study, ↓ absolute and relative testis and epididymis weights on day 41 Histopathological changes in the testis evident from day 21 onward (degenerating round spermatids, degenerating elongating spermatids, multinucleated giant cells in the testis, increased intraluminal aberrant cells in the epididymis). On day 41: elongating spermatids and Sertoli cell vacuolation in the testis and oligospermia in the epididymis also noted. ↓ epididymal sperm count (absolute/relative) from day 10-21; marked ↓ sperm count (absolute/relative) on day 41, ↑ abnormal sperm on day 21 and 41.	1314476
Reproductive toxicity in males: investigation of testicular/sperm toxicity with BYI08330-enol Oral gavage at 0, 800 mg/kg bw/day for 21 days	Rat	Effect levels not established. Clinical signs of toxicity in treated animals included localized soiled fur in anogenital region (4/5 rats) and mouth region (5/5 rats), salivation (5/5 rats) and reduced motor activity (2/5 rats). ↓ overall bwg, ↓ bw throughout treatment, ↓ food consumption during 1st and 2nd wk. Histopathological changes in testes (degeneration of round and elongating spermatids, diffuse sloughing of germ cells, presence of multinucleated giant spermatids, Sertoli cell vacuolation), ↑ abnormal sperm.	1314337

Study Type	Species	Results[1] (mg/kg bw/day in males/females)	Reference
Pharmacokinetics	Rat	Absorption: Rapidly and extensively absorbed (89–98% of total recovered radioactivity excreted via the renal route). No differences observed between sexes or between low dose (2 mg/kg bw), high dose (100 mg/kg bw) or repeated low dose tests. Between 91–100% of the administered doses (AD) were recovered in urine, feces and the body of animals. Distribution: Maximum plasma concentration was reached for all dose groups within 0.09 to 2.03 h after administration (calculated by pharmacokinetic modelling). Results from the high dose experiments indicated a sex difference in the maximum plasma concentration, which was significantly higher for males than for females. Radioactivity in tissues and organs at the 48-h termination were <0.2% for all dose groups. The highest concentrations were detected in the liver (0.002–0.18 mg/kg) and the kidney (0.001–0.11 mg/kg). Excretion: Urinary excretion was rapid (almost complete within 24 h) and was the major route of excretion (88–95% of AD) for both sexes and all dose regimens. Fecal elimination accounted for 2–11% of the AD. Metabolism: Parent compound was completely metabolized. Two main metabolites were detected in all samples. The main metabolic reaction was cleavage of the ester group resulting in the most prominent metabolite, BYI 08330-enol (53–87% of AD). All other metabolites could be derived from the enol intermediate. The second most prominent metabolite was BYI 08330-desmethyl-enol (5–37% of AD). Four more identified metabolites were of minor importance: BYI08330-ketohydroxy (0.5–1.1%), BYI08330-desmethyl-ketohydroxy (0.1–0.7%), BYI08330-enol GA (0.2–0.8%) and BYI08330-enol-alcohol (0.4–1.6%). A sex-related difference was noted in the quantitative distribution of the two main metabolites. The major metabolite (BYI08330-enol) was noted at lower quantities in males (53–66%) than in females (81–87%) and the second most prominent metabolite (BYI08330-desmethyl-enol) was higher in males (25–37%) compared to females (5–10%).	1314691

Study Type	Species	Results[1] (mg/kg bw/day in males/females)	Reference
Depletion of residues in male rats	Male rats received a single oral of 2 or 1000 mg/kg bw. Sacrificed at 1, 8 or 24 h after dosing.	Absorption and excretion: For the low dose group, absorption and excretion were rapid; excretion was primarily via the urine and nearly complete (112% of the administered dose) at 24 h post-dose. For the high dose group, the rates of absorption and excretion were lower, with only 27% of the dose excreted in the urine after 24 h. Distribution/target organ(s): For the low dose group, radioactivity in plasma and organs declined rapidly after dosing, resulting in low plasma residues at 24 h post-dose. For all time points, the residues in liver and kidney were lower than in plasma. For the high dose group, plasma radioactivity was slightly higher than in the liver and kidney, indicating saturation of transport mechanisms. Decline of tissue radioactivity was minimal from 1 to 8 h post-dose and increased only slightly between 8 and 24 h. The residues in testis, carcass and skin were lower than in plasma. Toxicologically significant compound(s): For the low dose group, the ratio of the two main metabolites, BYI 08330-enol and BYI 08330-desmethyl-enol, in urine was about 2:1. Due to its greater polarity, BYI 08330-desmethyl-enol was found at higher percentages in urine than in plasma and organs. The highest percentages of BYI 08330-desmethyl-enol were detected in liver, where the compound is formed by metabolic transformation of BYI 08330-enol. BYI 08330-desmethyl-enol levels in the plasma, kidney and testis were comparable but significantly lower than in liver. For the high dose group, BYI 08330-enol was the main metabolite. BYI 08330-desmethyl-enol occurred at slightly higher levels than in the low dose group. BYI 08330-desmethyl-enol levels were greater in urine than in plasma and organs. The highest percentage of BYI 08330-desmethyl-enol in tissues was detected in the liver and kidney. For all dose regimens, the most prominent metabolic reaction was the cleavage of the ester bond of the side chain yielding the BYI-08330-enol. The demethylation of the cyclohexyl-O-methyl group to the respective alcohol (BYI 08330-desmethyl-enol) was a further important metabolic reaction as well as the hydroxylation in the azaspir ring of BYI 08330-enol resulting in BYI 08330-ketohydroxy, which was mainly detected in liver and kidney. Other metabolic reactions (e.g. conjugation of the BYI 08330-enol with glucuronic acid (GA), oxidation of one of the methyl groups of the phenyl ring forming the BYI 08330-enol-alcohol, and demethylation of BYI 08330-keohydroxy to BYI 08330-desmethyl-ketohydroxy) were of minor importance.	1314448

Study Type	Species	Results[1] (mg/kg bw/day in males/females)	Reference
Autoradiography study	Rat Single oral dose of 3 mg/kg. One rat/sex sacrificed at 1, 4, 8, 24, 48, 72, 120, and 168 (male only) h post-dosing. Radioactivity in excreta and rat sections was determined.	BYI 08330 was rapidly absorbed and distributed among most organs and tissues within 1 h post-dosing. Excretion was primarily via the urine (104–113% of the administered dose) and was nearly complete within 48 h for males and 24 h for females. Urinary excretion within the first 1–4 h was much higher (8–10 times) for females than for males. Fecal excretion only accounted for 3–7% of the administered dose. Excretion of radioactivity via expired air was negligible (<0.01% of the administered dose). Highest concentrations of radioactivity were detected in the gastrointestinal tract, urinary bladder, kidney, liver and blood. Moderate concentrations were observed in the lung, myocardium, brown fat, skin, the major glands (adrenal, thyroid, salivary, pineal, pituitary) and the female reproductive organs. Tissue levels were generally higher for females compared to males. Peak values were observed 1 h post-dosing and declined to below the LOD within 48 h for male rats and 24 h for females.	1314291
Comparison of the in vitro metabolism in Liverbeads from male rat, mouse and human	Liverbeads from male rat (Wistar), mouse (CD1) and human were incubated for 4 h with [azaspirodecenyl-3-^{14}C] BYI 08330 at 50 or 520 µM.	The parent compound was completely metabolized and not detected in any of the species at both concentrations. At the low concentration, the enol metabolite was the predominant metabolite in all three species (87%, 66%, and 92% in the rat, mouse and human, respectively). The rat Liverbeads also produced the keto-hydroxy (3%), enol-alcohol (4%), and desmethyl-enol (1%) metabolites; no conjugation reaction occurred in the rat. The mouse Liverbeads also produced substantial amounts of the enol-glucuronide metabolite (30%) and minor amounts of the enol-alcohol (1%), desmethyl-enol (7%), and keto-hydroxy (2%) metabolites. The human Liverbeads also produced the enol-glucuronide (6%) and desmethyl-enol (1%) metabolites. The metabolites generated from the human Liverbeads were more comparable to those from the mouse than from the rat. In both the mouse and the human, conjugation was more prevalent than oxidative transformation. Evidence of metabolic saturation was observed at the high concentration. The enol metabolite was present in greater amounts (100%, 89% and 98% in the rat, mouse and human, respectively) and other metabolites were present in lower amounts or absent at the high concentration versus the low concentration.	1314585

Study Type	Species	Results[1] (mg/kg bw/day in males/females)	Reference
BYI08330-enol-glucoside (metabolite of BYI 08330 detected in fruiting and leafy crops) Pharmacokinetics	Rat (one male) Target dose of 0.1 mg/kg (actual dose of 0.063 mg/kg). Excreta and plasma were collected over 48 h and GIT, skin and carcass were analyzed at termination (48 h).	Absorption/Excretion: Absorption was rapid and commenced immediately after dosing. About half the dose was absorbed, based on the rate of renal excretion (53.3%) and the residue in the body without GIT (1.07%) at the time of sacrifice (48 h). Excretion was fast and almost complete 24 h after dose administration. Of the total excreted amount of 97.1%, 53.3% was via the urine and 43.7% was via the feces. Distribution: A negligible amount of radioactivity was noted in skin (0.09%) and GIT (0.11%). Radioactivity in the carcass amounted to 1% of the dose. Metabolism: Approximately 93% of the administered dose was quantified and identified. BYI 08330-enol was the main metabolite in excreta (64% of administered dose). Minor metabolites were BYI 08330-desmethyl-enol (5%) and BYI 08330-ketohydroxy (3%). Unchanged parent was detected in excreta at about 21% of the administered dose, most of which (20.7%) was found in feces.	1314311
BYI 08330-ketohydroxy (plant metabolite)	Rat (male) Single oral at a target dose level of 2 mg/kg bw and sacrificed after 48 h.	Rate and extent of absorption and excretion: Absorption and excretion were rapid. Approximately 55% of the administered dose was absorbed. Radioactivity in plasma peaked at 0.81 h post-dose. Excretion was almost complete within 24 h. After 48 h, approximately 54% of the administered dose was eliminated via the urine and 44% via the feces. Distribution/target organ(s): Less than 0.2% of the administered dose was detected in organs/tissues. Highest levels were associated with the gastrointestinal tract and liver. Toxicologically significant compound(s): BYI 08330-ketohydroxy was completely metabolized, was not detected in the urine, and was detected only in trace amounts in the feces. The primary metabolic reaction was the oxidative demethylation of the cyclo-hexyl-O-methyl group to the alcohol, BYI 08330-desmethyl-ketohydroxy. The remaining identified metabolites were mostly mono-, di-, and tri-oxygenated metabolites. Other metabolites were derived from the loss of two hydrogen atoms of the oxygenated metabolites to ‘dehydro’ derivates, which probably contain aldehyde or keto groups or carboxylic acid groups.	1314632

[1] Effects observed in males as well as females unless otherwise reported.

Table 4 Toxicology Endpoints for Use in Health Risk Assessment for Spirotetramat

Exposure Scenario	Dose (mg/kg bw/day)	Study	Endpoint	UF/SF[1] or Target MOE[2]
Acute dietary General population	NOAEL = 100 mg/kg bw/day	Acute neurotoxicity study in rats	Decrease in locomotor activity observed in males	100
	ARfD = 1 mg/kg bw			
Chronic dietary General population	NOAEL = 5 mg/kg bw/day	12-month dietary dog study	Brain effects (dilatation of brain ventricle) in both sexes and thymus effects (involution and decreased thymus size) in males	300
ADI (General Population) = 0.02 mg/kg bw/day				
Short-term dermal/inhalation	NOAEL = 32 mg/kg bw/day	90-day dog study	Clinical signs of toxicity, decreases in body weight gain and food consumption, effects on hematological parameters, thymus atrophy and decreased T_3 levels in females	300
Intermediate-term dermal/inhalation	NOAEL = 32 mg/kg bw/day	90-day dog study	Clinical signs of toxicity, decreases in body weight gain and food consumption, effects on hematological parameters, thymus atrophy and decreased T_3 levels in females	300

[1] Dietary scenarios
[2] Exposure scenarios

Table 5 Integrated Food Residue Chemistry Summary

NATURE OF THE RESIDUE IN APPLE		PMRA #1314313, 1314123
Matrix	Apple	Apple Cell Culture
Test site	Greenhouse	Laboratory
Treatment	Foliar	Direct application
Rate	1100 g a.i./ha/season	4045 kBq as total amount applied to 20 cell culture flasks
Timing of application	1) BBCH 69 (fruit setting); 2) BBCH 71 (second fruit fall)	
End-use product	Azaspirodecenyl-3-^{14}C-BYI 08330 formulated as an oil dispersion (100 OD)	
PHI	60 days	7 days
The majority of the radioactivity in apples treated foliarly was detected in the leaves. The majority of the TRR remained on the surface (48.5%), a further 49.5% of the TRR was found in extracts and only 2.1% of the TRR remained bound to solids. Parent was the major component of fruit surface residues and in the ACN/water extracts of leaves. From the apple cell culture experiment, it was ascertained that BYI 08330 is rapidly degraded by the apple cells to at least 14 minor components.		

Metabolites Identified	Total Radioactive Residues	
	Major Metabolites (>10% of the TRR)	Minor Metabolites (<10% of the TRR)
Apple-leaves (TRR = 36.63 ppm)	Spirotetramat, BYI 08330-enol	BYI 08330-ketohydroxy, BYI 08330-desmethyl-ketohydroxy-glucoside (isomers) + BYI 08330-ketohydroxy-formiate-glycoside
Apple-fruit (TRR = 0.61 ppm)	Spirotetramat, BYI 08330-mono-hydroxy	BYI 08330-ketohydroxy, BYI 08330-di-hydroxy, BYI 0833–desmethyl-ketohydroxy, BYI 08330-enol-glycoside, BYI 08330-enol
NATURE OF THE RESIDUE IN COTTON		PMRA #1314293
Matrix	Cotton	
Test site	Greenhouse	
Treatment	Foliar	
Rate	91.7 g a.i./ha (1st application); 172.3 g a.i./ha (2nd application) for a total of 264 g a.i./ha/season	
Timing of application	1) BBCH 15 (5th true leaf unfolded); 2) BBCH 85 (~50% of bolls open)	
End-use product	Azaspirodecenyl-3-^{14}C-BYI 08330 formulated as a suspension concentrate (240 SC)	
PHI	19 days and 39 days	
Samples of cotton gin trash, lint and undelinted seeds were harvested. As well, an immature cotton sample was harvested 19 days after the first application. Unchanged parent BYI 08330 was a major residue in the immature cotton sample, gin trash and lint. Degradation of the parent to BYI 08330-enol and BYI 08330-ketohydroxy was also widely observed in all RACs. Further hydroxylation of the metabolites led to the detection of BYI 08330-MA-amide in the immature cotton sample, gin trash and lint. Conjugation of several metabolites with glucose was observed in all RACs. Cleavage of the parent molecule was detected, resulting in the formation of BYI 08330-mandelic acid amide, the major metabolite of lint.		
Metabolites Identified	Total Radioactive Residues	
Cotton	Major Metabolites (>10% of the TRR)	Minor Metabolites (<10% of the TRR)
Intermediate (TRR = 2.381 ppm)	Spirotetramat	BYI 08330-ketohydroxy, BYI 08330-ketohydroxy-glucoside (isomers) BYI 08330-desmethyl-enol-Glc, BYI 08330-enol-Glc
Gin trash (TRR = 1.614)	Spirotetramat, BYI 08330-ketohydroxy, BYI 08330-enol	BYI 08330-enol-Glc, BYI 08330-keto hydroxy-Glc (isomer 2), BYI 08330-olefine (isomer 2)
Lint (TRR = 1.078 ppm)	Spirotetramat, BYI 08330-mandelic acid amide, BYI 08330-ketohydroxy	BYI 08330-enol, BYI 08330-olefine (isomer 1 and 2)
Undelinted Seeds (TRR=0.119 ppm)	BYI 08330-enol	BYI 08330-ketohydroxy, BYI 08330-enol-Glc, BYI 08330-desmethyl-enol-Glc
NATURE OF THE RESIDUE IN POTATO		PMRA #1314290
Matrix	Potato	
Test site	Greenhouse	
Treatment	Foliar	
Rate	102.7 g a.i./ha × 3 = 308 g a.i./ha/season; 21-day retreatment interval	
Timing of application	1) BBCH 75; 2) BBCH 85; 3) BBCH 93	
End-use product	Azaspirodecenyl-3-^{14}C-BYI 08330 formulated as an oil dispersion (100 OD)	
PHI	14 days	
Residues in potato tubers and leaves from treated plants were 0.255 ppm and 11.057 ppm, respectively. Approximately 85% and 87% of the total residues were identified in tubers and leaves, respectively. The major component of radioactive residues in tubers was identified as BYI 08330-enol (65.8% of the TRR), whereas in potato leaves the major components were identified as unchanged parent BYI 08330 (49.4% of the TRR) and BYI		

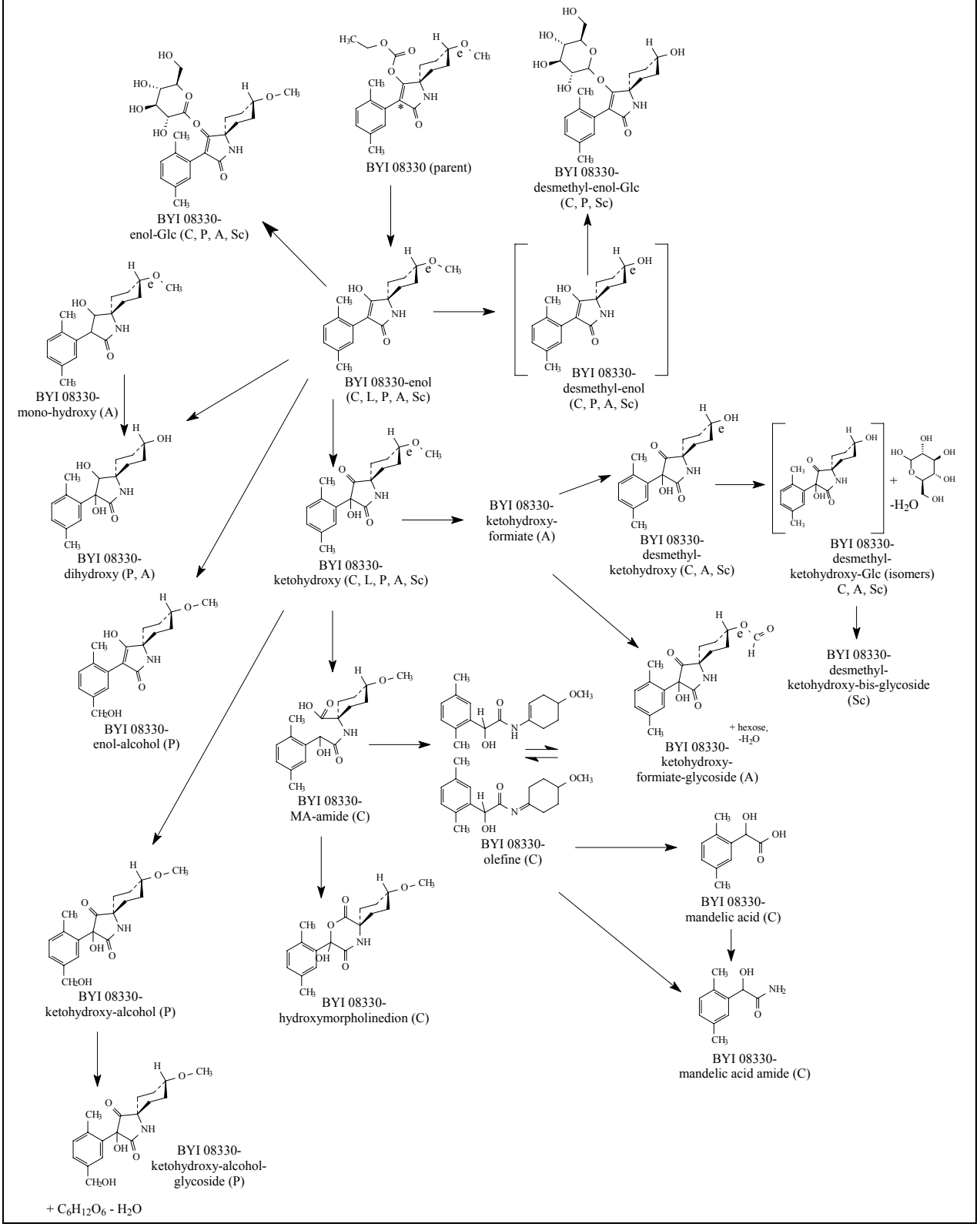
08330-ketohydroxy (24.8% of the TRR).		
Metabolites Identified	Total Radioactive Residues	
Potato	Major Metabolites (>10% of the TRR)	Minor Metabolites (<10% of the TRR)
Tubers (TRR = 0.255 ppm)	BYI 08330-enol	BYI 08330-desmethyl-enol, BYI 08330-ketohydroxy, BYI 08330-enol-glucoside
Leaves (TRR = 11.057 ppm)	Spirotetramat, BYI 08330-ketohydroxy	BYI 08330-enol, BYI 08330-enol-glucoside
NATURE OF THE RESIDUE IN LETTUCE		PMRA #1314184
Matrix	Lettuce	
Test site	Greenhouse	
Treatment	Foliar	
Rate	83.4 g a.i./ha × 2 = 167 g a.i./ha/season; 14-day retreatment interval	
Timing	1) BBCH 41; 2) BBCH 45-46	
End-use product	Azaspirodecenyl-3-^{14}C-BYI 08330 formulated as an oil dispersion (100 OD)	
PHI	7 days	
Total radioactive residues detected in lettuce were 3.13 ppm. The majority of radioactivity was extracted (98.7% of the TRR), and the majority of the radioactivity was identified as unchanged parent (55.9% of the TRR). Three other minor metabolites were identified as BYI 08330-enol, the glucose conjugate BYI 08330-enol-glucoside and BYI 08330-ketohydroxy. A number of other minor metabolites were characterized, each of which was present at <2% of the TRR; therefore, no further attempts at identification were undertaken.		
Metabolites Identified	Total Radioactive Residues	
Lettuce	Major Metabolites (>10% of the TRR)	Minor Metabolites (<10% of the TRR)
Lettuce heads TRR =3.13 ppm	Spirotetramat, BYI 08330-enol BYI 08330-enol-glucoside	BYI 08330-ketohydroxy

CONFINED ROTATIONAL CROP STUDY USING SPRING WHEAT, SWISS CHARD, TURNIPS			PMRA #1314701
Test site		Vegetation area - greenhouse	
Formulation used for trial		[Azaspirodecenyl-3-^{14}C] BYI 08330 applied to bare soil using a controlled track sprayer with a flat nozzle.	
Application rate and timing		One application at 406 g a.i./ha; 30 days, 135 days, 260 days prior to sowing Swiss chard, turnips and wheat.	
Metabolites Identified		Major Metabolites (>10% of the TRR)	Minor Metabolites (<10% of the TRR)
Matrix	PBI (days)	[Azaspirodecenyl-3-^{14}C] BYI 08330	[Azaspirodecenyl-3-^{14}C] BYI 08330
Wheat forage	30	Desmethyl-ketohydroxy-Glc, ketohydroxy	Desmethyl-di-hydroxy-Glc, ketohydroxy-alcohol-Glc, desmethyl-enol-alcohol, di-hydroxy, desmethyl-ketohydroxy-Glc-MA (isomer 1 & 2), desmethyl-ketohydroxy
Wheat hay	30	Desmethyl-ketohydroxy-Glc, desmethyl-ketohydroxy-Glc-MA, desmethyl-di-hydroxy, ketohydroxy-alcohol, desmethyl-ketohydroxy	Desmethyl-di-hydroxy-Glc, enol-Glc, desmethyl-di-hydroxy-Glc-MA, ketohydroxy-alcohol-Glc, desmethyl-ketohydroxy-Glc (isomer 1), desmethyl-enol-alcohol, di-hydroxy, desmethyl-ketohydroxy-Glc-MA (isomer 2), ketohydroxy, mandelic acid
Wheat straw	30	Desmethyl-di-hydroxy-Glc, desmethyl-di-hydroxy, ketohydroxy-alcohol, desmethyl-ketohydroxy	Enol-Glc, desmethyl-di-hydroxy-Glc-MA, ketohydroxy-alcohol-Glc, desmethyl-ketohydroxy-Glc (isomer 1 & 2), desmethyl-enol-alcohol, di-hydroxy, desmethyl-ketohydroxy-Glc-MA (isomer 1 & 2), ketohydroxy, mandelic acid

Wheat grain	30	-	Desmethyl-di-hydroxy-Glc, desmethyl-di-hydroxy, desmethyl-di-hydroxy-Glc-MA, ketohydroxy-alcohol-Glc, desmethyl-ketohydroxy-Glc (isomer 1 & 2), desmethyl-enol-alcohol, di-hydroxy, ketohydroxy-alcohol, desmethyl-ketohydroxy-Glc-MA (isomer 1 & 2), BYI 08330-enol, desmethyl-ketohydroxy
Swiss chard	30	Desmethyl-ketohydroxy-Glc, ketohydroxy, desmethyl-enol-alcohol, di-hydroxy, desmethyl-ketohydroxy	Desmethyl-di-hydroxy-Glc, desmethyl-di-hydroxy-Glc-MA, desmethyl-ketohydroxy-Glc (isomer 1 & 2), ketohydroxy-alcohol, ketohydroxy, desmethyl-di-hydroxy, mandelic acid
Turnip leaves	30	Ketohydroxy-alcohol	Desmethyl-di-hydroxy-Glc, desmethyl-di-hydroxy-Glc-MA, desmethyl-ketohydroxy-Glc (isomer 2), desmethyl-enol-alcohol, di-hydroxy, desmethyl-ketohydroxy-Glc-MA (isomer 2), desmethyl-ketohydroxy, ketohydroxy, desmethyl-di-hydroxy, mandelic acid, ketohydroxy-carboxylic acid
Turnip roots	30	BYI 08330-ketohydroxy	Desmethyl-di-hydroxy-Glc-MA, desmethyl-enol-alcohol, di-hydroxy, desmethyl-ketohydroxy
Wheat forage	135	Desmethyl-di-hydroxy-Glc	Desmethyl-di-hydroxy-Glc-MA, desmethyl-ketohydroxy-Glc (isomer 1 & 2), desmethyl-ketohydroxy-Glc-MA (isomer 1 & 2)
Wheat hay	135	Desmethyl-di-hydroxy-Glc, desmethyl-di-hydroxy-Glc-MA	Enol-Glc, ketohydroxy-alcohol-Glc, desmethyl-ketohydroxy-Glc (isomer 1 & 2), desmethyl-ketohydroxy-Glc-MA (isomer 1)
Wheat straw	135	BYI 08330-di-hydroxy	Desmethyl-di-hydroxy-Glc, enol-Glc, desmethyl-di-hydroxy, desmethyl-di-hydroxy-Glc-MA, ketohydroxy-alcohol-Glc, desmethyl-ketohydroxy-Glc (isomer 1 & 2), desmethyl-ketohydroxy-Glc-MA (isomer 1 & 2), desmethyl-ketohydroxy, ketohydroxy
Wheat grain	135	-	-
Swiss chard	135	BYI 08330-di-hydroxy, ketohydroxy	Desmethyl-di-hydroxy-Glc, desmethyl-di-hydroxy-Glc-MA, desmethyl-ketohydroxy-Glc (isomer 1 & 2), ketohydroxy-alcohol, desmethyl-ketohydroxy
Turnip leaves	135	-	Desmethyl-di-hydroxy-Glc, desmethyl-di-hydroxy-Glc-MA, desmethyl-ketohydroxy-Glc (isomer 2), ketohydroxy-alcohol, desmethyl-ketohydroxy
Turnip roots	135	-	-
Wheat hay	260	-	Desmethyl-di-hydroxy-Glc, desmethyl-di-hydroxy-Glc-MA, desmethyl-ketohydroxy-Glc (isomer 1 & 2), desmethyl-ketohydroxy-Glc-MA (isomer 1)
Wheat straw	260	BYI 08330-di-hydroxy	Desmethyl-di-hydroxy-Glc, desmethyl-di-hydroxy-Glc-MA, ketohydroxy-alcohol-Glc, desmethyl-ketohydroxy-Glc (isomer 1 & 2), desmethyl-ketohydroxy-Glc-MA (isomer 1 & 2), ketohydroxy

Wheat grain and forage	260	-	-
Swiss chard	260	-	-
Turnip leaves and roots	260	-	-
Major components identified in the confined rotational crop study included BYI08330, BYI08330-ketohydroxy, and free and conjugated BYI08330-desmethyl-ketohydroxy, BYI08330-desmethyl-di-hydroxy and BYI-08330-ketohydroxy-alcohol. Since none of these residues were found in the limited rotational crop field trials at a 30-day plantback interval, it is not necessary to consider these components as part of the residue definition for enforcement and risk assessment purposes at this time.			

Proposed Metabolic Scheme in Plants



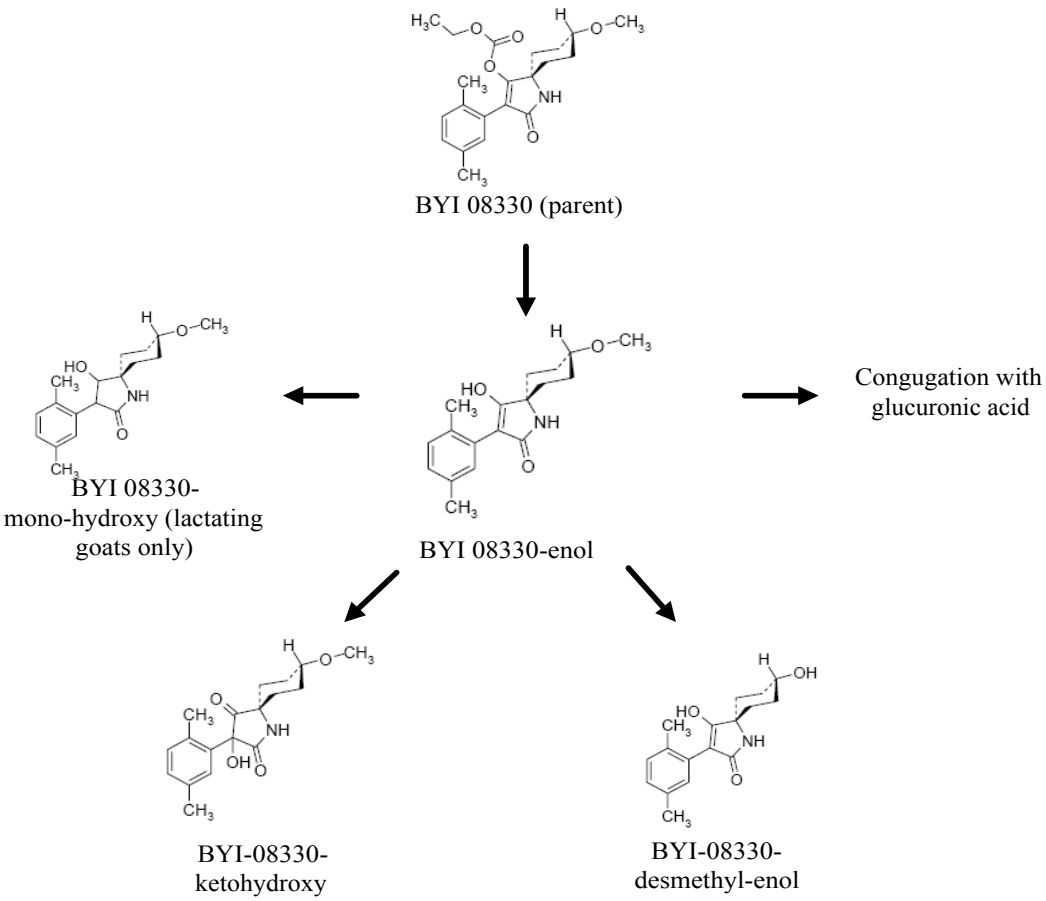
NATURE OF THE RESIDUE IN LAYING HEN		PMRA #1314288
Six laying hens were dosed orally with [azaspirodecenyl-3-^{14}C]cis-BYI 08330 for 14 consecutive days at a dose level of 1.01mg/kg body weight (corresponding to 12.86 ppm in the daily diet). Hens were sacrificed 24 h after the last dose and samples of organs and tissues were taken for analysis. Samples of eggs and excreta were collected daily for analysis. The majority of the administered dose was excreted rapidly. Residue levels in eggs and tissues were very low, with the highest concentrations of residues measured in kidneys, and liver.		
Matrices		% of the Administered Dose [Azaspirodecenyl-3-^{14}C]-BYI 08330
Excreta		90
Gastrointestinal tract contents		NA
Cage rinse		NA
Tissues and organs		0.023
Egg		0.045
Metabolites Identified	Total Radioactive Residues	
Radiolabel Position	Major Metabolites (>10% of the TRR)	Minor Metabolites (<10% of theTRR)
Muscle (TRR = 0.003 ppm)	BYI 08330-enol	BYI 08330-enol-GA, Unknown 1
Fat (TRR = 0.004 ppm)	BYI 08330-enol, Unknown 2	-
Liver (TRR = 0.017 ppm)	BYI 08330-enol, BYI 08330-enol-GA	Unknown 1
Kidney (TRR = 0.039 ppm)	Not further analyzed	Not further analyzed
Eggs (TRR = 0.015 ppm)	BYI 08330-enol	BYI 08330-enol-GA, Unknown 1

NATURE OF THE RESIDUE IN LACTATING GOAT		PMRA #1314289
A lactating goat received 4 daily oral doses of [azaspirodecenyl-3-^{14}C]-BYI08330 at an average dose rate of 2.22 mg/kg bw/day (73.03 ppm in feed) given by gavage. Milk samples were collected twice daily, urine and feces were collected once daily. The treated goat was sacrificed approximately 24 h after the last dosage, and muscle (round, flank, loin), fat (perirenal, omental subcutaneous), liver, kidneys were collected.		
Matrices		% of Administered Dose [Azaspirodecenyl-3-^{14}C]-BYI08330
Urine		78.4
Feces		11.6
Gastrointestinal tract contents		NA
Cage rinse		NA
Milk		0.014
Other tissues (muscle, fat, kidney, liver)		0.06
Metabolites Identified	Total Radioactive Residues	
Radiolabel Position	Major Metabolites (>10% of the TRR)	Minor Metabolites (<10% of the TRR)
Muscle	BYI 08330-enol	BYI 08330-ketohydroxy, BYI 08330-desmethyl-enol

Fat	BYI 08330-enol, BYI 08330-enol-GA	--
Liver	BYI 08330-enol-GA, BYI 08330-enol, unknown	BYI 08330-desmethyl-enol, BYI 08330-mono-hydroxy, BYI 08330-ketohydroxy
Kidney	BYI 08330-enol, BYI 08330-enol-GA	BYI 08330-desmethyl-enol, BYI 08330-ketohydroxy
Milk	BYI 08330-enol, BYI 08330-enol-GA	BYI 08330-desmethyl-enol, BYI 08330-mono-hydroxy, BYI 08330-ketohydroxy

The metabolism studies in ruminants and poultry were similar in that the majority of BYI 08330 was metabolized to BYI 08330-enol. As such, the residue definition in animal matrices is spirotetramat (BYI 08330) and the metabolite BYI 08330-enol.

Proposed Metabolic Scheme in Livestock



FREEZER STORAGE STABILITY IN PLANTS	PMRA #1480166

Samples of tomato (fruit and paste), potato (tuber), lettuce (head), climbing French bean (bean with pod) and almond (nutmeat) were spiked separately with 0.2 ppm of each spirotetramat (BYI 08330), BYI 08330-enol, BYI 08330-ketohydroxy, BYI 08330-mono-hydroxy, BYI 08330-enol-glucoside and stored at -18°C for approximately 30, 60, 90, 180, 370, 540 and 718 days. Spiked samples of orange juice and prunes were analyzed at 0-, 30-, 90- and 144/147-day intervals. All samples were analyzed by high-performance liquid chromatography with tandem mass spectrometry (HPLC-MS/MS) method 00857 using internal standards. Adequate method validation data were provided. Total residues of spirotetramat in tomato, potato, lettuce, climbing French bean and almond were stable (<30% degradation) during frozen storage for up to 718 days. Total residues of spirotetramat in orange juice and prunes were stable (<30% degradation) during frozen storage for up to 147 days.

FREEZER STORAGE STABILITY IN ROTATIONAL CROPS	PMRA #1314349

The purpose of this study was to assess the freezer storage stability of BYI 08330-ketohydroxy and all spirotetramat residues that can be converted by acid hydrolysis to BYI08330-desmethyl-ketohydroxy, BYI08330-desmethyl-di-hydroxy and BYI08330-ketohydroxy-alcohol in rotational crops. The samples of wheat (hay, straw and grain), Swiss chard and turnip (leaves and roots) from the confined rotational crop study were re-analyzed after a storage period of at least 30 months. A comparison of the metabolite profile of the confined rotational crop study samples, before and after storage, showed that the distribution of metabolites did not change during storage under frozen conditions. Residues were stable with 75–112% recoveries when comparing the residues in samples stored after 30–32 months with the same samples analyzed prior to storage.

CROP FIELD TRIALS ON POTATO	PMRA #1314451

GAP: Maximum seasonal rate of 175 g a.i/ha with a minimum interval of 7 days between applications and a PHI of 7 days.

Sixteen field trials were completed to investigate the magnitude of total BYI 08330 residues in potatoes treated with two foliar applications of BYI 08330 150 OD or 240 SC. An appropriate number of trials were conducted in the representative NAFTA growing regions. Each formulation was applied at a rate of 0.086-0.092 kg a.i./ha with a retreatment interval of 5 to 7 days for a total seasonal application rate of 0.173-0.180 kg a.i./ha. All applications were made using spray volumes of 121 to 191 L/ha and Dyne-Amic (0.5% v/v) as an adjuvant. Potato tubers were harvested 7 days after the last application. Decline experiments were performed at two different sites in order to ascertain changes in the magnitude of residues with time. The total residues of spirotetramat declined when the PHI increased from 3 to 20 days, but it was only observed at one site. Total spirotetramat residues were higher with the 150 OD formulation in comparison to the 240 SC formulation.

Commodity	Total Rate (kg a.i./ha)	PHI (days)	Total Spirotetramat Residue Levels (ppm)						
			n	Min.	Max.	HAFT	Median	Mean	Std. Dev.
Potato - 150 OD	0.173–0.180	7	32	<0.050	0.457	0.450	0.119	0.171	0.125
Potato - 240 SC		7	8	<0.060	0.139	0.138	0.075	0.087	0.032

CROP FIELD TRIALS ON *BRASSICA* LEAFY VEGETABLES	PMRA #1314488

GAP: Maximum seasonal rate of 175 g a.i./ha with a minimum interval of 7 days between applications and a PHI of 1 day.

A total of 20 field trials were conducted in representative commodities of Crop Subgroup 5A (broccoli (3), cauliflower (3) and cabbage (6)), and Crop Subgroup 5B (mustard greens (8)). A decline trial was conducted with broccoli, cabbage and mustard greens. An appropriate number of trials were conducted in the representative NAFTA growing regions. BYI 08330 100 OD or BYI 08330 240 SC was applied at target rates of 88 g a.i./ha/application at intervals of 5–7 days for a total seasonal application rate of 171–184 g a.i./ha (BYI 08330 100 OD) and 174–176 g a.i./ha (BYI 08330 240 SC). All applications were made using spray volumes of 102 to 188 L/ha and Dyne-Amic (0.5% v/v) as an adjuvant. Total residues of spirotetramat were generally higher in commodities treated with the 100 OD formulation in comparison to the 240 SC formulation. There was no clear decline of total BYI 08330 residues in broccoli/cauliflower treated with either the 100 OD or 240 SC formulated products. Decline of total BYI 08330 residues was only observed in cabbage heads with wrapper leaves treated with the 100 OD formulation. Total BYI 08330 residues in mustard greens declined with time when treated with the 240 SC formulation.

Commodity	Total Rate (kg a.i./ha)	PHI (days)	Total Spirotetramat Residue Levels (ppm)						
			n	Min.	Max.	HAFT	Median	Mean	Std. Dev.
Broccoli/Cauliflower									
Flower head and stems	100 OD 0.173–0.177	1	13	0.099	0.451	0.423	0.369	0.336	0.110
	240 SC 0.176	1	4	0.210	0.325	0.307	0.289	0.278	0.048
Cabbage									
Heads with wrapper leaves	100 OD 0.173–0.177	1	12	0.054	0.924	0.911	0.312	0.394	0.317
	240 SC 0.176	1	2	0.050	0.050	0.050	0.050	0.050	N/A
Heads without wrapper leaves	100 OD 0.173–0.177	1	10	0.052	0.170	0.164	0.095	0.097	0.041
	240 SC 0.176	1	2	0.055	0.056	0.056	0.056	0.056	N/A
Mustard Greens									
Greens	100 OD 0.171–0.184	1	17	0.771	5.490	5.358	3.378	2.795	1.708
	240 SC 0.174 –0.176	1	4	0.784	4.460	4.400	2.600	2.611	2.066

CROP FIELD TRIALS ON CUCURBITS — PMRA #1314489

GAP: Maximum seasonal rate of 175 g a.i./ha with a minimum interval of 7 days between applications and a PHI of 1 day.

A total of 17 field trials were conducted in representative commodities of Crop Group 9 (cucumber, muskmelon and summer squash). An appropriate number of trials were conducted in the representative NAFTA growing regions. Two broadcast foliar applications of either BYI 08330 100 OD or BYI 08330 240 SC were applied at a target rate of 88 g a.i./ha/application, with a retreatment interval of 5–7 days. Total seasonal application rates for all trials ranged from 165 to 181 g a.i./ha for BYI 08330 100 OD and from 173 to 179 g a.i./ha for BYI 08330 240 SC. All spray mixtures included Dyne-Amic (0.5% v/v) as an adjuvant. Samples of each commodity were collected one day after the last application. In the decline trials, samples were collected at five intervals corresponding to PHIs of approximately 0, 1, 3, 7 and 10 days. Total spirotetramat residue levels were similar in cucumbers and muskmelons treated with the 100 OD or 240 SC formulations. However, total spirotetramat residues were higher in summer squash treated with the 100 OD formulation. There was no apparent decline of residues in cucumber and muskmelon. However, a decline of residues was observed in summer squash when treated with the OD formulation from a 1-day PHI to a 7-day PHI.

Commodity	Total Rate (kg a.i./ha)	PHI (days)	Total Spirotetramat Residue Levels (ppm)						
			n	Min.	Max.	HAFT	Median	Mean	Std. Dev.
Cucumber - 100 OD	0.165–0.181	1	12	<0.050	0.076	0.075	0.050	0.057	0.011
Cucumber - 240 SC	0.173–0.179	1	4	<0.050	0.057	0.054	0.050	0.052	0
Muskmelon 100 OD	0.165–0.181	1–2	12	<0.050	0.134	0.098	0.054	0.063	0.024
Muskmelon - 240 SC	0.173–0.179	1–2	4	<0.050	0.163	0.113	0.060	0.083	0.053
Summer Squash - 100 OD	0.165–0.181	1	10	<0.050	0.184	0.173	0.069	0.095	0.051

Summer Squash - 240 SC	0.173–0.179	1	2	<0.050	0.051	0.051	—	—	—

CROP FIELD TRIALS ON LEAFY VEGETABLES	PMRA #1314487

GAP: Maximum seasonal rate of 175 g a.i./ha with a minimum interval of 7 days between application and a PHI of 3 days.

A total of 24 field trials were conducted in order to investigate the magnitude of total BYI 08330 residues in/on representative commodities of Crop Group 4 (head and leaf lettuce, celery, and spinach). An appropriate number of trials were conducted in the representative NAFTA growing regions.Trials were conducted with either a 100 OD formulation or a 240 SC formulation being applied twice at a target rate of 88 g a.i./ha with 5 to 8 days between treatments. The total seasonal application rate was 0.171–0.183 g a.i./ha. All applications were made using spray volumes of 83 to 189 L/ha and Dyne-Amic (0.5%) as an adjuvant. Samples of head lettuce, leaf lettuce, celery and spinach were harvested 3 days after the last treatment. In the decline trials, samples were collected at 0-, 1-, 3-, 7- and 10-day PHIs. Total spirotetramat residues declined with increasing PHIs in head lettuce, leaf lettuce, celery and spinach. Residues were higher in leaf lettuce, celery and spinach when treated with the 100 OD formulation. Residue levels were similar in head lettuce (with and without wrapper leaves) when treated with the 100 OD or 240 SC formulated products.

Commodity	Total Rate (kg a.i./ha)	PHI (days)	Total Spirotetramat Residue Levels (ppm)						
			n	Min.	Max.	HAFT	Median	Mean	Std. Dev.
Head Lettuce	0.171–0.183 100 OD	3 (with wrapper leaves)	12	0.197	0.918	0.822	0.708	0.605	0.261
		3 (without wrapper leaves)	10	0.111	0.385	0.383	0.167	0.203	0.101
Head Lettuce	0.171–0.181 240 SC	3 (with wrapper leaves)	4	0.173	1.035	0.957	0.583	0.593	0.427
		3 (without wrapper leaves)	4	0.160	0.241	0.234	0.224	0.212	0.036
Leaf Lettuce	0.171–0.183 100 OD	3	12	0.188	1.676	1.604	0.831	0.882	0.449
	0.171–0.181 240 SC	3	2	0.211	0.227	0.219	0.219	0.219	NA
Celery	0.171–0.183 100 OD	3	15	0.248	2.633	2.533	0.606	1.019	0.856
	0.171–0.181 240 SC	3	4	0.402	0.490	0.465	0.424	0.435	0.040
Spinach	0.171–0.183 100 OD	3	14	0.204	3.360	3.071	1.334	1.493	0.977
	0.171–0.181 240 SC	3	2	2.338	2.654	2.496	2.496	2.496	NA

CROP FIELD TRIALS ON CITRUS	PMRA #1314490

US GAP: Two foliar sprays at 0.18 kg a.i./ha/application with a minimum retreatment interval of 21 days, for a maximum seasonal rate of 0.36 kg a.i./ha and a PHI of 1 day.

During the 2005 growing season, trials were conducted on representative commodities of Crop Group 10 (orange, lemon, grapefruit). An appropriate number of trials were conducted in the representative NAFTA growing regions. Two ground-based airblast spray applications of either BYI08330 150 OD or BYI08330 240 SC were made at rates that ranged from 0.168 to 0.187 kg a.i./ha/application, for a total seasonal rate of from 0.344 to 0.360 kg a.i./ha/season. The interval between applications ranged from 14 to 21 days. All spray mixtures included Dyne-Amic adjuvant (0.25% v/v). Samples of oranges, lemons and grapefruits were harvested at a preharvest interval (PHI) of 1 day. In decline trials, samples were collected at five intervals corresponding to PHIs of 0, 1, 7, 10 and 14 days. Additional orange samples were collected to determine the effect of peeling. Most of the residues in oranges appeared to be associated with the peel since the levels decreased to below the LOQ when the peel was removed. Total spirotetramat residue levels were similar in commodities treated with the BYI 08330 150 OD formulation and the BYI 08330 240 SC formulation. However, total spirotetramat residues (maximum values) were higher in commodities treated with the concentrated spray. In decline trials, detectable residues dissipated slightly with increasing PHIs in orange, with no apparent decline in grapefruit and lemon.

Commodity	Total Rate (kg a.i./ha)	PHI (days)	Total Spirotetramat Residue Levels (ppm)						
			n	Min.	Max.	HAFT	Median	Mean	Std. Dev.
Orange -150 OD	0.344–0.360	1	51	0.250	0.433	0.427	0.298	0.306	0.054
Orange - 240 SC		1	6	0.250	0.413	0.388	0.307	0.315	0.064
Lemon - 150 OD	0.344–0.360	1	20	0.251	0.465	0.456	0.300	0.321	0.063
Lemon - 240 SC		1	2	0.305	0.392	0.348	—	—	—
Grapefruit - 150 OD	0.344–0.360	1	24	0.250	0.351	0.344	0.250	0.260	0.027
Grapefruit - 240 SC		1	4	0.250	0.250	0.250	0.250	0.250	0

CROP FIELD TRIALS ON FRUITING VEGETABLES	PMRA #1314516

GAP: Maximum seasonal rate of 175 g a.i./ha with a minimum interval of 7 days between applications and a PHI of 1 day.

A total of 21 trials were conducted in or on representative commodities of Crop Group 8 (tomatoes, bell and non-bell peppers). An appropriate number of trials were conducted in the representative NAFTA growing regions. At each test location, two broadcast foliar applications of BYI08330 100 OD or BYI08330 240 SC were made to tomatoes, bell peppers or chili peppers at a target rate of 88 g a.i./ha/application for a total seasonal rate that ranged from 0.168 to 0.199 kg a.i./ha. Retreatment intervals were 5 to 7 days with a preharvest interval of 1 day. All spray mixtures included Dyne-Amic adjuvant. Total spirotetramat residue levels were higher in fruiting vegetables treated with the 100 OD formulation in comparison to the 240 SC formulation. In decline studies, samples were collected at PHIs of 0, 1, 3, 7 and 10 days. There was no clear trend of decline observed in the total spirotetramat residues (maximum values) in tomato, bell pepper or non-bell pepper.

Commodity	Total Rate (kg a.i./ha)	PHI (days)	Total Spirotetramat Residue Levels (ppm)						
			n	Min.	Max.	HAFT	Median	Mean	Std. Dev.
Tomato – 100 OD	0.168–0.199	1	24	0.060	0.227	0.214	0.137	0.139	0.049
Tomato – 240 SC		1	6	0.072	0.189	0.177	0.139	0.130	0.048
Bell pepper -100 OD	0.168–0.199	1	12	0.156	0.682	0.655	0.299	0.351	0.182
Bell pepper - 240 SC	0.168–0.199	1	4	0.188	0.361	0.275	0.259	0.267	0.080
Chili pepper -100 OD	0.168–0.199	1	6	0.427	1.379	1.232	0.558	0.748	0.390

CROP FIELD TRIALS ON GRAPES	PMRA #1314622

GAP: Maximum seasonal rate of 220 g a.i./ha with a minimum interval of 30 days between applications and a PHI of 7 days.

A total of 12 trials were conducted on grapes during the 2005 growing season. An appropriate number of trials were conducted in the representative NAFTA growing regions.Test substance BYI 08330-150 OD or 240 SC was applied as a ground-based foliar spray at rates that ranged from 0.109 to 0.114 kg a.i./ha/application. The interval between applications ranged from 28 to 30 days. Total seasonal application rates for all trials ranged from 0.219 to 0.227 kg a.i./ha. All applications were made in spray volumes of 458 to 654 L/ha and used Dyne-Amic (0.25% v/v) as an adjuvant. Samples were collected 7 days after the last application. In a decline trial, grapes treated with the 150 OD formulation were collected at five intervals corresponding to PHIs of 3, 7, 10, 14 and 21 days. Total spirotetramat residues were higher with the 150 OD formulation in comparison to the 240 SC formulation. Total spirotetramat residues did not appear to dissipate when the PHI increased from 3 to 21 days.

Commodity	Total Rate (kg a.i./ha)	PHI (days)	Total Spirotetramat Residue Levels (ppm)						
			n	Min.	Max.	HAFT	Median	Mean	Std. Dev.
Grape - 150 OD	0.219–0.227	7	24	0.109	1.290	1.024	0.329	0.406	0.257
Grape - 240 SC	0.219–0.227	7	6	0.187	0.547	0.466	0.347	0.348	0.130

CROP FIELD TRIALS ON HOPS	PMRA #1314494

GAP: Maximum seasonal rate of 220 g a.i./ha with a minimum interval of 14 days between applications and a PHI of 7 days.

Three field trials were conducted during the 2005 growing season. An appropriate number of trials were conducted in the representative NAFTA growing regions. At each test location, BYI08330 150 OD or BYI08330 240 SC was applied twice as a postemergent foliar spray at a rate of 0.108 to 0.112 kg a.i./ha/application with a retreatment interval of 12 to 14 days. The total application rate was from 0.218 to 0.224 kg a.i./ha/season. All spray mixtures included Dyne-Amic (0.25% v/v) as an adjuvant. Hop cones were harvested at a preharvest interval of 7 days. Decline trials were conducted with samples collected at 7 and 14 days after the last application. Total spirotetramat residues were higher with the 150 OD formulation in comparison to the 240 SC formulation. Total spirotetramat residues declined slightly when the PHI increased from 7 to 14 days.

Commodity	Total Rate (kg a.i./ha)	PHI (days)	Total Spirotetramat Residue Levels (ppm)						
			n	Min.	Max.	HAFT	Median	Mean	Std. Dev.
Hops - 150 OD	0.218–0.224	7	6	2.164	5.820	5.492	5.167	4.427	1.675
Hops - 240 SC	0.218–0.224	7	2	3.149	4.512	3.830	—	—	—

CROP FIELD TRIALS ON POME FRUIT	PMRA #1314492

GAP: Maximum seasonal rate of 440 g a.i./ha with a minimum interval of 14 days between applications and a PHI of 7 days.

A total of 18 field trials were conducted on the representative commodities of Crop Group 11 (apples and pears) during the 2005 growing season. An appropriate number of trials were conducted in the representative NAFTA growing regions. Applications of spirotetramat were made with one of two end-use products, BYI 08330 150OD or BYI 08330 240 SC. Applied rates were 0.155 to 0.167 kg a.i./ha for the first application and 0.134 to 0.145 kg a.i./ha for the second and third applications, for a total of 0.430 to 0.447 kg a.i./ha/season with a 14-day retreatment interval. All spray mixtures included Dyne-Amic adjuvant. Apples and pears were collected 7 days following the final application. Decline trials were conducted on apples and pears with samples collected at preharvest intervals of 0, 7, 14 and 21 days. Total spirotetramat residues were higher in apples and pears treated with the 150 OD formulation. However, total spirotetramat residues were not significantly different between the application spray volumes (concentrated and dilute). Total spirotetramat residues in/on pome fruit declined with time.

Commodity	Total Rate (kg a.i./ha)	PHI (days)	Total Spirotetramat Residue Levels (ppm)						
			n	Min.	Max.	HAFT	Median	Mean	Std. Dev.
Apple - 150 OD	0.430–0.447	7	44	0.052	0.375	0.344	0.126	0.148	0.090
Apple - 240 SC	0.430–0.447	7	6	0.062	0.144	0.143	0.075	0.094	0.039
Pear -150 OD	0.430–0.447	7	22	0.063	0.373	0.344	0.175	0.177	0.086
Pear - 240 SC	0.430–0.447	7	4	0.137	0.259	0.250	0.196	0.197	0.062
CROP FIELD TRIALS ON STONE FRUIT					PMRA #1314485				
GAP: Maximum seasonal rate of 270 g a.i./ha with a minimum interval of 14 days between applications and a PHI of 7 days.									
A total of 21 trials were conducted on the representative commodities of Crop Group 12 (cherries, peaches, plums). An appropriate number of trials were conducted in the representative NAFTA growing regions. At each test location, two airblast spray applications of BYI08330 150 OD or BYI08330 240 SC were made at rates from 0.156 to 0.165 kg a.i./ha/application for the first application and 0.107 to 0.112 kg a.i./ha/application for the second application for a total seasonal rate that ranged from 0.265 to 0.274 kg a.i./ha. All spray mixtures included the adjuvant Dyne-Amic (0.25% v/v).The retreatment interval was 12 to 15 days with a preharvest interval of 7 days. Decline trials were conducted with each commodity and the samples were collected at PHIs of 0, 7, 10, 14 and 21 days. Total spirotetramat residues were higher in cherries, peaches and plums treated with the 150 OD compared to the 240 SC formulated products. The maximum total residues in plums were higher when treated with the concentrated spray. Total spirotetramat residues declined with increasing PHIs in cherries, but not in peaches or plums.									
Commodity	Total Rate (kg a.i./ha)	PHI (days)	Total Spirotetramat Residue Levels (ppm)						
			n	Min.	Max.	HAFT	Median	Mean	Std. Dev.
Cherries - 150 OD	0.265–0.274 Concentrated	7	12	0.318	2.120	2.016	1.315	1.266	0.548
	0.265–0.274 Dilute	7	12	0.222	2.127	2.044	1.602	1.480	0.564
Cherries - 240 SC	0.265–0.274 Concentrated	7	2	0.572	0.645	0.608	0.608	0.608	-
Peaches - 150 OD	0.265–0.274 Concentrated	7	24	0.273	1.227	1.034	0.432	0.496	0.211
	0.265–0.274 Dilute	7	14	0.414	1.142	1.109	0.692	0.692	0.217
Peaches - 240 SC	0.265–0.274 Concentrated	7	6	0.339	0.809	0.668	0.560	0.539	0.178
Plum - 150 OD	0.265–0.274 Concentrated	7	12	0.059	0.373	0.306	0.225	0.237	0.107
	0.265–0.274 Dilute	7	12	0.091	0.842	0.683	0.212	0.313	0.243
Plum - 240 SC	0.265–0.274 Concentrated	7	2	0.060	0.065	0.062	0.062	0.062	-

CROP FIELD TRIALS ON TREE NUTS						PMRA #1314621			
GAP: Maximum seasonal rate of 380 g a.i./ha with a minimum interval of 14 days between applications and a PHI of 7 days.									
Ten field trials were conducted on the representative commodities of Crop Group 14 (almonds and pecans). An appropriate number of trials were conducted in the representative NAFTA growing regions. At each test location, three ground-based airblast spray applications of either BYI08330 150 OD or BYI08330 240 SC were made to tree nuts at rates that ranged from 0.155 to 0.162 kg a.i./ha/application for the first application, and from 0.107 to 0.114 kg a.i./ha/application for the second and third applications. Total seasonal application rates ranged from 0.369 to 0.386 kg a.i./ha with application intervals of 12 to 20 days and a preharvest interval of 7 days. All spray mixtures included Dyne-Amic (0.25% v/v) as an adjuvant. Decline trials were conducted with samples collected at 0, 6, 10, 13 and 21 days after the last application. Total spirotetramat residue levels were higher in tree nuts treated with the 150 OD formulation. However, there was no significant difference observed in total spirotetramat residues in tree nuts treated with concentrated or dilute spray volumes. Residues did not decline in almond or pecan nutmeat with increasing PHIs.									
Commodity	Total Rate (kg a.i./ha)	PHI (days)	Total Spirotetramat Residue Levels (ppm)						
			n	Min.	Max.	HAFT	Median	Mean	Std. Dev.
Almond nutmeats - 150 OD	0.369–0.386	7	20	0.050	0.143	0.128	0.075	0.081	0.031
Almond nutmeats - 240 SC		7	4	0.063	0.083	0.078	0.072	0.072	0.008
Almond hulls - 150 OD	0.369–0.386	7	20	1.261	5.145	4.988	2.466	2.931	1.333
Almond hulls - 240 SC		7	4	1.923	5.260	4.579	2.919	3.255	1.627
Pecans - 150 OD	0.369–0.386	7	20	0.050	0.297	0.295	0.053	0.105	0.087
Pecans - 240 SC		7	2	0.052	0.078	0.065	—	—	—
CROP FIELD TRIALS ON STRAWBERRIES						Annex B.7.6 of EU Dossier			
EU GAP: Two foliar sprays at 0.095 kg a.i./ha/application, for a maximum seasonal rate of 0.19 kg a.i./ha with a retreatment interval of 14 days and a PHI of 3 days.									
Sixteen residue trials were conducted on strawberries treated with BYI 08330 100 OD formulation in a greenhouse (Germany and France) and under field conditions (N-EU: Germany and N-France; S-EU: Italy, Spain and S-France). The submitted field trial data are adequate to fulfill the data requirements for strawberries imported from Europe. The last application was carried out at growth stage BBCH 81-89. Samples were taken before the last treatment at 0, 1, 3 and 7 and 14-15 days after the last application. Total residues of spirotetramat did not appear to decline significantly with time. Residue levels were higher in the trials conducted in a greenhouse as opposed to the field trials.									
Commodity	Total Rate (kg a.i./ha)	PHI (days)	Total Spirotetramat Residue Levels (ppm)						
			n	Min.	Max.	HAFT	Median	Mean	Std. Dev.
Greenhouse trials	0.19	3–7	8	0.172	0.328	0.328	0.282	0.271	0.040
Field - N. Europe		3–7	4	0.130	0.258	0.258	0.1987	0.204	0.042
Field - S. Europe		3–7	4	0.108	0.152	0.143	0.143	0.138	0.017
CROP FIELD TRIALS ON ONIONS						Annex B.7.6 of EU Dossier			
EU GAP: Four foliar sprays at 0.072 kg a.i./ha/application, for a maximum seasonal rate of 0.29 kg a.i./ha with a retreatment interval of 7 days and a PHI of 7 days.									
Eight residue trials for each European region (Northen and Southern) were conducted using oil-based dispersion concentrates containing 150 g/L and 100 g/L of spirotetramat, respectively. The submitted field trial data are adequate to fulfill the data requirements for onions imported from Europe. The product was used four times, using an application rate of 0.072 kg a.i./ha. The last application was carried out at BBCH growth stage 47-48. Samples of onion bulbs were taken at 0, 3, 7, 14 and 21 days after the last application. There was no apparent decline of total spirotetramat residues over time.									

Commodity	Total Rate (kg a.i./ha)	PHI (days)	Total Spirotetramat Residue Levels (ppm)						
			n	Min.	Max.	HAFT	Median	Mean	Std. Dev.
Field - N. and S. Europe	0.29	7, 14, 21	16	0.054	0.202	0.202	0.0975	0.109	0.011

PROCESSED FOOD AND FEED	PMRA #1314446, 1314450, 1314610, 1314400, 1314587, 1314445, 1314452

Processing studies were conducted on orange, grape, plum, potato, hops and tomato samples. Additional samples were taken for peaches, peppers and oranges during the magnitude of the residue trials to assess the effect of washing, peeling or cooking. Experimental values obtained were typically lower or conformed with the theoretical factors.

RAC	Processed Commodity	Experimental Processing Factor
Apple	Wet Pomace	1.9
	Juice	0.4
	Washed Fruit	0.6
	Peeled Fruit	0.2
	Applesauce	0.1
	Dried Fruit	1
Fresh Grapes	Washed Grapes	0.60
	Raisins	2.61
	Juice	0.66
	Jelly	0.28
Plum	Prunes	2.2
	Washed Fruit	0.9
Cherries	Washed Fruit	1.1
	Cooked	1.0
Tomato	Whole Washed Fruit	0.7
	Paste	7.4
	Purée	3.5
	Fruit, Cooked	0.6
	Juice	0.9
	Preserve	1.1
	Fruit, Dried	11.8
Potato Tuber	Washed Potatoes	1.2
	Peeled Potato Tuber	1.1
	Cooked Potatoes	1.3
	Potato Wet Peel	0.97
	Potato Chips	1.2
	Potato Flakes	3.5
Peppers	Washed	1.3
	Cooked	1.2
Orange Whole Fruit	Orange Juice	0.40
	Orange Dried Pulp	1.27
	Orange Oil	13.5
Grapefruit	Washed and waxed	0.10
Lemon	Lemon Juice	0.40
	Lemon Peel	1.0
Peach	Peach, Washed	0.40
	Peach Juice	0.40
	Peach, Cooked	0.20
	Dried Peach	2.90

LIVESTOCK FEEDING STUDY	PMRA #1314447

Spriotetramat was administered via capsule to 10 lactating Holstein dairy cows for 29 consecutive days. The target dose rates (based on feed dry weight) were 0 mg/kg feed/day (control), 3.0 mg/kg feed/day, 9.0 mg/kg feed/day, or 30 mg/kg feed/day. Milk was collected twice daily during the dosing period. Additionally, a portion of the 26-day milk sample from the 30 ppm dose group was separated into milk fat (cream) and whey (skim milk), and each was analyzed. The animals were sacrificed on day 29 and samples of liver, kidney, muscle and fat were collected for analysis. Samples were analyzed for total spirotetramat residues (BYI 08330 + BYI 08330-enol + BYI 08330-enol-glucuronide).

Matrix	Feeding Level (ppm)	Total Spirotetramat Residue Levels (ppm) (BYI 08330 + BYI 08330-enol + BYI 08330-enol-glucuronide)					
		n	Min.	Max.	Median	Mean	Std. Dev.
Milk	30	30	<0.005	0.006	<0.005	<0.005	0.0006
Milk fat	30	3	<0.005	<0.005	<0.005	<0.005	-
Whey	30	3	<0.005	<0.005	<0.005	<0.005	-
Fat	3	3	<0.010	<0.010	<0.010	<0.010	-
Fat	9	3	<0.010	0.017	<0.010	0.0123	0.004
Fat	30	3	<0.010	0.038	0.037	0.0283	0.016
Kidney	3	3	0.021	0.025	0.021	0.022	0.002
Kidney	9	3	0.051	0.103	0.070	0.075	0.026
Kidney	30	3	0.184	0.437	0.200	0.274	0.142
Muscle	3	3	<0.010	<0.010	<0.010	<0.010	-
Muscle	9	3	<0.010	<0.010	<0.010	<0.010	-
Muscle	30	3	<0.010	0.016	0.011	0.012	0.003
Liver	3	3	<0.010	<0.010	<0.010	<0.010	-
Liver	9	3	0.013	0.018	0.016	0.016	0.003
Liver	30	3	0.031	0.057	0.032	0.040	0.015

Calculation of Livestock Maximum Dietary Burden in Beef, Dairy, Poultry and Swine

The potential for secondary transfer of total spirotetramat residues in meat, meat byproducts and milk exist because there are livestock feedstuffs associated with the proposed uses on apples, citrus, potatoes and almonds. The calculated maximum dietary burden, based on RAC MRLs or the HAFT value and processing factor, is 0.88 ppm (beef cattle), 1.0 ppm (dairy cattle), and 0 ppm (swine and poultry).

				% Diet				Residue (ppm)			
Feedstuff	Type	Residues (ppm)	% DM	Beef	Dairy	Poultry	Swine	Beef	Dairy	Poultry	Swine
Almond hulls	R	9.0	90	-	10	-	-	-	1.0	-	-
Apple, wet pomace	R	0.65*	40	-	10	-	-	-	0.16	-	-
Citrus, dried pulp	R	0.58*	88	10	10	-	-	0.066	0.066	-	-
Untreated forage/silage/hay/ other	R	NA	-	30	20	-	-	-	-	-	-
Potato, processed waste	CC	0.44*	15	30	10	-	-	0.88	0.29	-	-
Untreated grain/grain milled byproduct/other	CC	NA	-	20	30	80	80	-	-	-	-
Untreated oilseed meal	PC	NA	-	10	10	20	20	-	-	-	-
Totals				100	100	100	100	0.88	1.0	0	0

R (roughage); CC (carbohydrates); PC (protein concentrate)
Shaded boxes indicate values that are not considered since these feedstuffs are generated in limited supply seasonally and/or locally, but not in the same geographical areas. Therefore, only 1 out of 4 values inputted is considered; i.e. the one that gives the highest dietary burden.
* RAC (HAFT × Processing Factor)

Calculation of the Anticipated Residues for Dietary Exposure Assessment					
Matrix	Maximum Total Residues[3] (ppm)	Feeding Level (ppm)	Transfer Coefficient [1]	Dietary Burden (ppm)	Anticipated Residues[2] (ppm)
Milk & milk fat	0.011	30	0.00037	1.0	0.00037
Fat	0.038	30	0.0013	0.88	0.0011
Muscle	0.016	30	0.00053	0.88	0.00047
Kidney	0.437	30	0.0146	0.88	0.013
Liver	0.057	30	0.0019	0.88	0.0017

[1] Transfer coefficient is calculated as residue level-to-feed ratios.
[2] Anticipated residue for dietary exposure assessment = Transfer coefficient × dietary burden.
[3]Maximum Total Residues = sum of BYI 08330 + BYI 08330-enol + BYI 08330-enol-glucuronide.

Table 6 Overview of Nature of Residue Studies and Dietary Exposure Assessment

PLANT STUDIES					
RESIDUE DEFINITION FOR ENFORCEMENT AND RISK ASSESSMENT Primary crops: Potato, Cotton, Apple, Lettuce	Spirotetramat (BYI08330), BYI08330-enol, BYI08330-ketohydroxy, BYI08330-monohydroxy, and BYI08330 enol-glucoside, expressed as BYI08330 equivalents.				
METABOLIC PROFILE IN DIVERSE CROPS	Similar in the crops evaluated.				
Rotational crops	Major components identified in the confined rotational crop study included BYI08330, BYI08330-ketohydroxy, and free and conjugated BYI08330-desmethyl-ketohydroxy, BYI08330-desmethyl-di-hydroxy and BYI-08330-ketohydroxy-alcohol. Since none of these residues were found in the limited rotational crop field trials at a 30-day PBI, they are not included in the residue definition for enforcement and risk assessment purposes.				
ANIMAL STUDIES					
ANIMALS	Goat and Hen				
RESIDUE DEFINITION FOR ENFORCEMENT	BYI 08330 and BYI08330-enol, expressed as BYI08330 equivalents.				
RESIDUE DEFINITION FOR RISK ASSESSMENT	BYI08330, BYI08330-enol and BYI08330-enol-glucuronide, expressed as BYI08330 equivalents.				
METABOLIC PROFILE IN ANIMALS (goat, hen, rat)	The metabolic profile was similar in all animals investigated.				
FAT SOLUBLE RESIDUE	NO				
Chronic Assessment: **ADI** = 0.02 mg/kg bw **EEC** = 0.0032 µg/L (Level 1) Acute Assessment: **ARfD** = 1.00 mg/kg bw **EEC** = 0.0105 µg/L (Level 1)	Population	Estimated Acute Risk (% of ARfD) 95th percentile		Estimated Chronic Risk (% of ADI)	
		Refined Food	Refined Food & Water	Refined Food	Refined Food & Water
	General population	0.4	0.5	7.0	7.3
	All infants (<1 year)	0.7	0.7	9.4	10.5
	Children 1–2 yrs	1.1	1.1	20.0	20.5
	Children 3–5 yrs	0.8	0.9	15.3	15.8
	Children 6–12 yrs	0.5	0.5	8.8	9.1

	Youth 13–19 yrs	0.3	0.3	5.6	5.8
	Adults 20–49 yrs	0.3	0.4	5.6	5.9
	Adults 50+ yrs	0.4	0.4	6.1	6.4
	Females 13–49 yrs	0.3	0.4	5.5	5.8

Table 7 Major Environmental Transformation Products of Spirotetramat

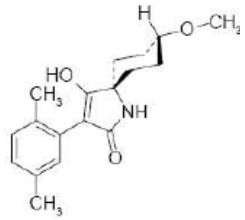
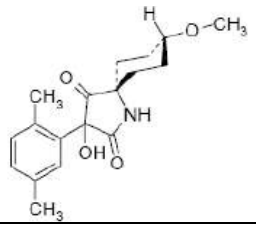
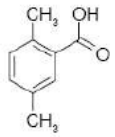
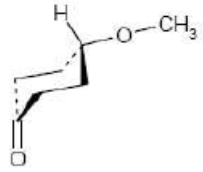
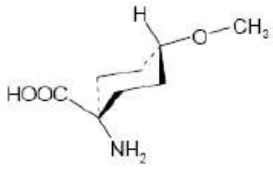
Substance	Chemical Name	Structure	Molecular Mass (g/mole)	Occurrence (max % AR)
Spirotetramat-enol	CAS: cis-3-(2,5-Dimethylphenyl)-4-hydroxy-8-methoxy-1-azaspiro[4.5]dec-3-en-2-one		301.4	Aerobic soil (worst-case assumption): 100 Anaerobic soil: 54.6 Soil photolysis: 10.1 Hydrolysis: 91.8 Water photolysis: 81.9 Aerobic water/sed: 79.7/41.2 Anaerobic water/sed: 100
Spirotetramat-ketohydroxy	CAS: cis-3-(2,5-Dimethylphenyl)-3-hydroxy-8-methoxy-1-azaspiro[4.5] decan-2,4-dione		317.4	Aerobic soil: 24.0 Anaerobic soil: 19.3 Soil photolysis: 20.9 Hydrolysis : - Water photolysis: - Aerobic water/sed: 17.4/42.8 Anaerobic water/sed: -
Dimethyl-benzoic acid	IUPAC: 2,5-Dimethyl-benzoic acid		150.2	Aerobic soil: - Anaerobic soil: - Soil photolysis: 21.8 Hydrolysis: - Anaerobic water/sed: -
Methoxy-cyclohexanone	CAS: 4-methoxy-cyclohexanone		128.2	Aerobic soil: - Anaerobic soil: - Soil photolysis: 10.0 Hydrolysis: - Water photolysis: 17.5 Aerobic water/sed: - Anaerobic water/sed: -
Methoxy-cyclohexylaminocarboxylic acid	CAS: Cyclohexanecarboxylic acid		173.2	Aerobic soil: - Anaerobic soil: - Soil photolysis: - Hydrolysis: - Water photolysis: 11.3 Aerobic water/sed: - Anaerobic water/sed: -

Table 8 Fate and Behaviour in the Environment

Property	Test Substance	Value	Comments	Reference
Terrestrial Environment				
Abiotic transformation				
Hydrolysis	Spirotetramat	Half-life (d): pH 4: 47.6 (20°C), 32.5 (25°C), 5.69 (50°C) pH 7: 13.1 (20°C), 8.60 (25°C), 0.62 (50°C) pH 9: 0.32 (25°C), 0.14 (30°C)	Expected to be an important route of transformation in alkaline conditions	1314408
	Spirotetramat-enol	Stable		1314444
Phototransformation on soil	Spirotetramat	Half-life not available	Not expected to be an important route of transformation	1314480
Phototransformation in air	Spirotetramat	No data required	Not volatile (based on the vapour pressure and Henry's law constant)	No data required
Biotransformation				
Biotransformation in aerobic soil	Spirotetramat	DT_{50} ($t_{1/2}$): 0.10–0.38 days[1] DT_{90} : 0.34–1.26 days	Non-persistent	1314287
	Spirotetramat-enol	DT_{50} ($t_{1/2}$): 3.3–12.3 days[1] DT_{90} : 10.9–40.9 days	Non-persistent	1314324
	Spirotetramat-ketohydroxy	DT_{50} ($t_{1/2}$): 1.5–16.7 days[2] DT_{90} ($t_{9/10}$): 5.1–55.6 days[2]	Non-persistent	1314692
Biotransformation in anaerobic soil	Spirotetramat	DT_{50} ($t_{1/2}$): 0.25 days[3] DT_{90} ($t_{9/10}$): 0.83 days[3]	Non-persistent	1314325
Mobility				
Adsorption/ desorption in soil	Spirotetramat	K_{oc}: 184–437 K_d: 3.58–5.52	Moderately mobile	1314478
	Spirotetramat-enol	K_{oc} not determined	See leaching study for K_{oc}	1314317
	Spirotetramat-ketohydroxy	K_{oc}: 42–99.7	High to very high mobility	1314645
Soil leaching	Spirotetramat-enol	No residues found below 12 cm in column; 0.1–2.8% found in leachates Estimated K_{oc}: 27–99	 High to very high mobility	1314479
	Spirotetramat-ketohydroxy	Residues found in all column layers (up to 30 cm); 0.2–7.5% found in leachates		1314479
Volatilization	Spirotetramat	No data required	Not volatile (based on the vapour pressure and Henry's law constant)	No data required

Property	Test Substance	Value	Comments	Reference
Field studies				
Field dissipation (New York)	Spirotetramat 100 OD	Spirotetramat: DT_{50}: 0.5 days DT_{90}: 1.6 days Combined spirotetramat-enol + spirotetramat-ketohydroxy: DT_{50}: 31.6 days DT_{90}: 105 days Residues of spirotetramat and its transformation products not found below 15 cm	Non-persistent	1314513
Field dissipation (Washington)	Spirotetramat 100 OD	Spirotetramat: DT_{50}: 0.3–0.4 days DT_{90}: 1.1–1.4 days Combined spirotetramat-enol + spirotetramat-ketohydroxy: DT_{50}: 4.6–5.2 days DT_{90}: 15.4–17.4 days Residues of spirotetramat and its transformation products not found below 15 cm	Non-persistent	1314511
Aquatic Environment				
Abiotic transformation				
Hydrolysis	Spirotetramat	Half-life (d): pH 4: 47.6 (20°C), 32.5 (25°C), 5.69 (50°C) pH 7: 13.1 (20°C), 8.60 (25°C), 0.62 (50°C) pH 9: 0.32 (25°C), 0.14 (30°C)	Expected to be an important route of transformation in alkaline conditions	1314408
	Spirotetramat-enol	Stable		1314444
Phototransformation in water	Spirotetramat	DT_{50}: 20.2 days (pH 5) 1.05 days (pH 7.9)	Under a midday summer light in Edmonton. Values are based on the net experimental half-life of 3 days (in pH 5 buffer) and 0.22 day (in natural water at pH 7.9).	1314172 1314173

Biotransformation				
Biotransformation in aerobic water systems	Spirotetramat	DT_{50} ($t_{1/2}$): 1.05–1.06 days DT_{90} ($t_{9/10}$): 3.50–3.52 days	Whole system (in water phase, $t_{1/2}$ was 1.00–1.02 d) Non-persistent	1314305
	Spirotetramat-enol	DT_{50} ($t_{1/2}$): 37.9–59.0 days[2] DT_{90} ($t_{9/10}$): 126–196 days[2]	Slightly to moderately persistent	1314637
	Spirotetramat-ketohydroxy	Stable[2]	Persistent	1314637
Biotransformation in anaerobic water systems	Spirotetramat	DT_{50} ($t_{1/2}$): 2.8 days DT_{90} ($t_{9/10}$): 9.3 days	Whole system (in water phase, $t_{1/2}$ was also 2.8 d) Non-persistent	1314255

[1] The first order half-life ($t_{½}$) was estimated by dividing the DT_{90} (from DFOP best fit kinetics) by 3.32.
[2] First order half-life values obtained from multi-compartmental modelling.
[3] For entire system. Values obtained from single first order kinetics. Other values were also obtained using other calculation methods: DT_{50} = 0.06 d and DT_{90} = 1.33 d using FOMC (best-fit), DT_{50} = 0.22 d and DT_{90} = 0.87 using DFOP.

Table 9 Toxicity to Non-Target Species

Organism	Type of Exposure	Test Substance	Endpoint Value	PMRA #
Terrestrial Organisms				
Invertebrates				
Earthworm (Eisenia fetida)	Acute	Spirotetramat	14-d LC_{50}: >1000 mg a.i./kg soil	1314410
	Acute	Spirotetramat-ketohydroxy	14-d LC_{50}: >1000 mg/kg soil	1314332
	Chronic	Spirotetramat-enol	8-wk NOEC: 32 mg/kg soil (reproduction)	1314333
Bee (Apis mellifera)	Oral	Spirotetramat	48-h LD_{50}: >107.3 µg a.i./bee; equivalent to >120 g a.i./ha[1]	1314159
		Spirotetramat 150 OD	48-h LD_{50}: 91.7 µg a.i./bee; equivalent to 103 g a.i./ha[1]	1314312
	Contact	Spirotetramat	48-h LD_{50}: >100 µg a.i./bee; equivalent to >112 g a.i./ha[1]	1314159
		Spirotetramat 150 OD	48-h LD_{50}: 162 µg a.i./bee; equivalent to 181 g a.i./ha[1]	1314312
	Semi-field/ Field	Spirotetramat 150 OD (feeding test)	Slightly increased mortality of adults and pupae. No effect on flight activity, bee behaviour. Brood development: high termination rate in two of three colonies. No recovery until the end of the observation period.	1314546
		Spirotetramat 240 SC (feeding test)	Increased adult mortality. No effects on flight activity and behaviour of bees. Brood development: termination of brood development with tendency to recover.	1314545

Organism	Type of Exposure	Test Substance	Endpoint Value	PMRA #
		Spirotetramat 150 OD (semi-field study)	No adverse effects on adult and brood mortality, condition of the colonies, flight activity and behaviour of bees.	1314627
		Spirotetramat 150 OD (semi-field study, tunnel test)	No adverse effects on adult and brood mortality, condition of the colonies, flight activity and behaviour of bees. Brood development: irritation of brood development in the earlier assessments in one of 3 colonies of the 5× treatment. Recovery.	1314322
		Spirotetramat 150 OD (semi-field study, tunnel test)	Brood development: reduction of larval abundance, with recovery.	1470102
Parasitoid wasp (Aphidius rhopalosiphi)	Contact	Spirotetramat 150 OD (on glass plates)	48-h LR_{50}: 114.7 g a.i./ha	1314366
		Spirotetramat 150 OD (on treated leaves)	48-h LR_{50}: >288 g a.i./ha	1314387
Predatory mite (*Typhlodromus pyri*)	Contact	Spirotetramat 150 OD (on glass plates)	48-h LR_{50}: 0.33 g a.i./ha	1314157
		Spirotetramat 150 OD (on treated leaves)	7-d LR_{50}: 1.59 g a.i./ha	1314372
Green lacewing (Chrysoperla carnea)	Contact	Spirotetramat 150 OD (on treated leaves)	48-h LR_{50}: >288 g a.i./ha	1314260
Ladybird beetle (Coccinella septempunctata)	Contact	Spirotetramat 150 OD (on treated leaves)	48-h LR_{50}: >288 g a.i./ha	1314386
Birds				
Northern bobwhite quail (*Colinus* virginianus)	Acute	Spirotetramat	LD_{50}: >2000 mg a.i./kg bw NOEL: <500 mg a.i./kg bw (feed consumption, diarrhea, soft excrement); 1000 mg a.i./kg bw (mortality)	1314205
	Dietary	Spirotetramat	5-d LC_{50}: >4998 mg a.i./kg diet; equivalent to 5-d LD_{50} of >497 mg a.i./kg bw/day[2] NOEC: 1250 mg a.i./kg diet (food avoidance); 1998 mg a.i./kg diet (mortality)	1314204
	Reproduc-tion	Spirotetramat	NOEC: 264 mg a.i./kg diet (mean hatchling body weight); equivalent to a NOEL of 23 mg a.i./kg bw/day[2]	1314666

Organism	Type of Exposure	Test Substance	Endpoint Value	PMRA #
Mallard duck (Anas platyrhynchos)	Dietary	Spirotetramat	5-d LC_{50}: >6050 mg a.i./kg diet; equivalent to 5-d LD_{50} of >475 mg a.i./kg bw/day[2] NOEC: <344 mg a.i./kg diet (food avoidance, reduced body weight gain); 6050 mg a.i./kg diet (mortality)	1314376
	Reproduc-tion	Spirotetramat	NOEC: 28.8 mg a.i./kg diet (foot lesions in adults, offspring body weight, egg production and hatchability); equivalent to a NOEL of 4.0 mg a.i./kg bw/day [2]	1314697
Mammals				
Rat	Acute	Spirotetramat	LD_{50}: >2000 mg a.i./kg bw	1314092
		Spirotetramat 150 OD	LD_{50}: >2000 mg a.i./kg bw	1314158 1314219
		Spirotetramat 240 SC	LD_{50}: >2000 mg a.i./kg bw	1314220
	Dietary	Spirotetramat	90-d NOEL: 2500 ppm (adverse effects on testes and spermatozoa); equivalent to 148 mg a.i./kg bw/day[2]	1314138
	Reproduc-tion (multi-generation)	Spirotetramat	NOEL: 1000 ppm (decrease in offspring body weight); equivalent to 71 mg a.i./kg bw/day[2]	1314542
Mouse	Dietary	Spirotetramat	90-d NOEL: 7000 ppm (no treatment-related effects); equivalent to 1305 mg a.i./kg bw/day[2]	1314367
Vascular plants				
Vascular plant	Seedling emergence	Spirotetramat 150 OD	EC_{25}: >176 g a.i./ha (all tested species, all parameters)	1314582
	Vegetative vigour	Spirotetramat 150 OD	EC_{25}: 76 g a.i./ha (corn, dry weight); 168 g a.i./ha (ryegrass, dry weight)	1314457
Aquatic organisms				
Freshwater species				
Water flea (*Daphnia magna*)	Acute	Spirotetramat	48-h EC_{50}: >42.7 mg a.i./L (immobility) NOEC: 20.3 mg a.i./L (immobility)	1314404
		Spirotetramat-enol	48-h EC_{50}: >100 mg/L (immobility) NOEC: 100 mg/L (immobility)	1314303
		Methoxycyclo hexanone	48-h EC_{50}: >100 mg/L (immobility) NOEC: 100 mg/L (immobility)	1314339
	Chronic	Spirotetramat	21-d NOEC: 2.0 mg a.i./L (adult mortality); 5.0 mg a.i./L (reproduction); 5.0 mg a.i./L (adult growth)	1314411
Midge (Chironomus riparius)	Acute (1st instar larvae)	Spirotetramat	48-h LC_{50}: 1.30 mg a.i./L NOEC: <0.56 mg a.i./L (mortality)	1314477
		Spirotetramat - enol	48-h LC_{50}: 74.9 mg/L NOEC: 17.1 mg/L (mortality)[3]	1314348
		Spirotetramat - ketohydroxy	48-h LC_{50}: >100 mg/L NOEC: 23.9 mg/L (mortality)[3]	1314471
		Methoxycyclo hexanone	48-h LC_{50}: >100 mg/L NOEC: 100 mg/L (mortality)	1419915
		Methoxycyclo hexylamincarb oxylic acid	48-h LC_{50}: >100 mg/L NOEC: 100 mg/L (mortality)	1419914

Organism	Type of Exposure	Test Substance	Endpoint Value	PMRA #
		Spirotetramat 150 OD	48-h LC_{50}: 0.66 mg a.i./L NOEC: 0.41 mg a.i./L (mortality)[3]	1314343
	Chronic[4] (1st instar larvae)	Spirotetramat	28-d NOEC: 0.1 mg a.i./L (emergence); 0.8 mg a.i./L (development)	1314380
Rainbow trout (Oncorhynchus mykiss)	Acute	Spirotetramat	96-h LC_{50}: 2.54 mg a.i./L NOEC: 0.825 mg a.i./L (mortality)	1314412
		Spirotetramat-enol	96-h LC_{50}: >100 mg/L NOEC: 100 mg/L (mortality)	1314308
		Spirotetramat 150 OD	96-h LC_{50}: 1.41 mg a.i./L NOEC: 0.38 mg a.i./L (mortality)	1314328
Zebra fish (*Danio rerio*)	Acute	Methoxycyclo hexanone	96-h LC_{50}: >100 mg/L NOEC: 100 mg/L (mortality)	1314346
Common carp (Cyprinodon carpio)	Acute	Spirotetramat	96-h LC_{50}: 2.59 mg a.i./L NOEC: 1.02 mg a.i./L (mortality)	1314319
Bluegill sunfish (*Lepomis macrochirus*)	Acute	Spirotetramat	96-h LC_{50}: 2.2 mg a.i./L NOEC: 0.5 mg a.i./L (mortality)	1314403
Fathead minnow (Pimephales promelas)	Chronic	Spirotetramat	33-d NOEC: 1.16 mg a.i./L (hatchability); 0.534 mg a.i./L (fry survival); 1.16 mg a.i./L (growth)	1314426
Green algae (*P. subcapitata*)	Acute	Spirotetramat	72-h EC_{50}: 6.58 mg a.i./L (biomass); 8.15 mg a.i./L (growth rate) NOEC: 1.46 mg a.i./L (biomass, growth rate)	1314203
		Spirotetramat-enol	72-h EC_{50}: >100 mg/L (biomass, growth rate) NOEC: 31 mg/L (biomass, growth rate)	1314345
		Spirotetramat 150 OD	72-h EC_{50}: 6.56 mg a.i./L (biomass); >8.2 g a.i./L (growth rate) NOEC: 2.02 mg a.i./L (biomass, growth rate)	1314342
Green algae (*D. subspicatus*)	Acute	Methoxycyclo hexanone	72-h EC_{50}: >100 mg/L (biomass, growth rate) NOEC: 100 mg/L	1314566
Blue-green algae (*Anabaena flos-aqua*)	Acute	Spirotetramat	96-h EC_{50}: 15.2 mg a.i./L (biomass); >15.1 mg a.i./L (growth rate) NOEC: 5.68 mg a.i./L (biomass); 15.1 mg a.i./L (growth rate)	1314363
Diatom (Navicular pellicullosa)	Acute	Spirotetramat	96-h EC_{50}: 4.05 mg a.i./L (biomass); 15.0 mg a.i./L (growth rate) NOEC: 0.19 mg a.i./L (biomass); 1.00 mg a.i./L (growth rate)	1314153
Vascular plant (*Lemna gibba*)	Dissolved	Spirotetramat	7-d EC_{50}: 4.49 mg a.i./L (yield); 6.21 mg a.i./L (growth rate) NOEC: 1.54 mg a.i./L (yield, growth rate)	1314280
		Spirotetramat-enol	7-d EC_{50}: 5.4 mg/L (yield); 19.3 mg/L (growth rate) NOEC: 0.95 mg/L (yield); 3.05 mg/L (growth rate)	1314347

Organism	Type of Exposure	Test Substance	Endpoint Value	PMRA #
Marine species				
Mysid shrimp (Americamysis bahia)	Acute	Spirotetramat	96-h LC_{50}: 5.5 mg a.i./L NOEC: <0.73 mg a.i./L (mortality)	1314271
Eastern oyster (Crassostrea virginica)	Acute	Spirotetramat	96-h EC_{50}: 0.85 mg a.i./L (shell deposition) NOEC: 0.33 mg a.i./L	1314375
Sheepshead minnow (Cyprinodon variegatus)	Acute	Spirotetramat	96-h LC_{50}: 1.96 mg a.i./L NOEC: 0.582 mg a.i./L (mortality)	1314368
Diatom (Skeletonema costatum)	Acute	Spirotetramat	96-h EC_{50}: 0.36 mg a.i./L (biomass); 0.96 mg a.i./L (growth rate) NOEC: 0.124 mg/L (biomass, growth rate)	1314379

[1] Toxicity in µg/bee converted to the equivalent kg a.i./ha using a conversion factor of 1.12 (Atkins *et al.*, 1981)
[2] Endpoints reported as concentrations in diet were converted to daily doses: Daily Dose = Toxicity × FIR × 1/bw, where the average food ingestion rate (FIR) and body weight (bw) were drawn from study.
[3] LC_{10} (a NOEC was not determined)
[4] Not a true chronic test: spiked water system

Table 10 Screening Level Risk Assessment on Non-target Species (Excluding Birds and Mammals)

Organism	Type of Exposure	Test Substance	Toxicity	Exposure (EEC) [1]	RQ [2]
Terrestrial organisms					
Invertebrates					
Earthworm	Acute	Spirotetramat	LC_{50}/2: >500 mg a.i./kg soil	0.062 mg a.i./kg soil	<0.00012
		Spirotetramat-ketohydroxy	LC_{50}/2: >500 mg/kg soil	0.095 mg/kg soil	<0.00019
	Chronic	Spirotetramat-enol	NOEC: 32 mg/kg soil	0.080 mg/kg soil	0.0025
Bee	Oral	Spirotetramat	LD_{50}: >107.3 µg a.i./bee (i.e. >120 g a.i./ha)	0.156 kg a.i./ha	<0.0013
		Spirotetramat 150 OD	LD_{50}: 91.7 µg a.i./bee (i.e. 103 g a.i./ha)	0.156 kg a.i./ha	0.0015
	Contact	Spirotetramat	LD_{50}: >100 µg/bee (i.e. >112 g a.i./ha)	0.156 kg a.i./ha	<0.0014
		Spirotetramat 150 OD	LD_{50}: 162 µg a.i./bee (i.e. 181 g a.i./ha)	0.156 kg a.i./ha	0.001
Parasitoid wasp	Contact	Spirotetramat 150 OD	LR_{50}: 114.7 g a.i./ha	77.8 g a.i./ha	0.6785
Predatory mite	Contact	Spirotetramat 150 OD	LR_{50}: 0.33 g a.i./ha	77.8 g a.i./ha	235.83
Green lacewing	Contact	Spirotetramat 150 OD	LR_{50}: >288 g a.i./ha	77.8 g a.i./ha	<0.2702

Organism	Type of Exposure	Test Substance	Toxicity	Exposure (EEC) [1]	RQ [2]
Ladybird beetle	Contact	Spirotetramat 150 OD	LR_{50}: >288 g a.i./ha	77.8 g a.i./ha	<0.2702
Vascular plants					
Vascular plant	Seedling emergence	Spirotetramat 150 OD	EC_{25}: >176 g a.i./ha	155.6 g a.i./ha	<0.8844
	Vegetative vigour	Spirotetramat 150 OD	EC_{25} (corn): 76 g a.i./ha	155.6 g a.i./ha	2.048
			EC_{25} (ryegrass): 168 g a.i./ha	155.6 g a.i./ha	0.9265
Aquatic organisms					
Freshwater species					
Daphnia	Acute	Spirotetramat	48-h EC_{50}/2: >21.35 mg a.i./L	0.0175 mg a.i./L	<0.0008
		Spirotetramat-enol	48-h EC_{50}/2: >50 mg/L	0.0365 mg/L	<0.0007
		Methoxycyclohexanone	48-h EC_{50}/2: >50 mg/L	0.0189 mg/L	<0.0004
	Chronic	Spirotetramat	21-d NOEC: 2.0 mg a.i./L	0.0175 mg a.i./L	0.0088
Midge	Acute	Spirotetramat	48-h LC_{50}/2: 0.65 mg a.i./L	0.0175 mg a.i./L	0.0269
		Spirotetramat - enol	48-h LC_{50}/2: 37.45 mg/L	0.0365 mg/L	0.001
		Spirotetramat - ketohydroxy	48-h LC_{50}/2: >50 mg/L	0.0468 mg/L	<0.00064
		Methoxycyclohexanone	48-h LC_{50}/2: >50 mg/L	0.0189 mg/L	<0.00038
		Methoxycyclohexylaminocarboxylic acid	48-h LC_{50}/2: >50 mg/L	0.0256 mg/L	<0.00051
		Spirotetramat 150 OD	48-h LC_{50}/2: 0.33 mg a.i./L	0.0175 mg a.i./L	0.053
	Chronic	Spirotetramat	28-d NOEC: 0.1 mg a.i./L	0.0175 mg a.i./L	0.175
Rainbow trout	Acute	Spirotetramat	96-h LC_{50}/10: 0.25 mg a.i./L	0.0175 mg a.i./L	0.0689
		Spirotetramat-enol	96-h LC_{50}/10: >10 mg/L	0.0365 mg/L	<0.0036
		Spirotetramat 150 OD	96-h LC_{50}/10: 0.14 mg a.i./L	0.0175 mg a.i./L	0.1241
Zebra fish	Acute	Methoxycyclohexanone	96-h LC_{50}/10: >10 mg/L	0.0189 mg/L	<0.0019
Common carp	Acute	Spirotetramat	96-h LC_{50}/10: 0.26 mg a.i./L	0.0175 mg a.i./L	0.0676
Bluegill sunfish	Acute	Spirotetramat	96-h LC_{50}/10: 0.22 mg a.i./L	0.0175 mg a.i./L	0.0796
Fathead minnow	Chronic	Spirotetramat	33-d NOEC: 0.534 mg a.i./L	0.0175 mg a.i./L	0.0328
Green algae	Acute	Spirotetramat	72-h EC_{50}/2: 3.29 mg a.i./L	0.0175 mg a.i./L	0.0053
		Spirotetramat-enol	72-h EC_{50}/2: >50 mg/L	0.0365 mg/L	<0.0007

Organism	Type of Exposure	Test Substance	Toxicity	Exposure (EEC) [1]	RQ [2]
		Methoxycyclohexanone	72-h EC_{50}/2: >50 mg/L	0.0189 mg/L	<0.0004
		Spirotetramat 150 OD	72-h EC_{50}/2: 3.28 g a.i./L	0.0175 mg a.i./L	0.0053
Blue-green algae	Acute	Spirotetramat	96-h EC_{50}/2: 7.6 mg a.i./L	0.0175 mg a.i./L	0.0023
Diatom	Acute	Spirotetramat	96-h EC_{50}/2: 2.03 g a.i./L	0.0175 mg a.i./L	0.0086
Vascular plant	Dissolved	Spirotetramat	7-d EC_{50}/2: 2.25 mg a.i./L	0.0175 mg a.i./L	0.0078
		Spirotetramat-enol	7-d EC_{50}/2: 2.7 mg/L	0.0365 mg/L	0.0135
Amphibians					
Amphibians	Acute (based on acute fish studies)	Spirotetramat	96-h LC_{50}/10: 0.22 mg a.i./L (bluegill sunfish)	0.0933 mg a.i./L	0.4241
		Spirotetramat-enol	96-h LC_{50}/10: >10 mg/L (rainbow trout)	0.195 mg/L	0.0195
		Methoxycyclohexanone	96-h LC_{50}/10: >10 mg/L (zebra fish)	0.101 mg/L	0.0101
		Spirotetramat 150 OD	96-h LC_{50}/10: 0.14 mg a.i./L (rainbow trout)	0.0933 mg a.i./L	0.6617
	Chronic (based on early life stage fish study)	Spirotetramat	33-d NOEC: 0.534 mg a.i./L (fathead minnow)	0.0933 mg a.i./L	0.1747
Marine species					
Mysid shrimp	Acute	Spirotetramat	96-h LC_{50}/2: 2.75 mg a.i./L	0.0175 mg a.i./L	0.0064
Eastern oyster	Acute	Spirotetramat	96-h EC_{50}/2: 0.43 mg a.i./L	0.0175 mg a.i./L	0.0412
Sheepshead minnow	Acute	Spirotetramat	96-h LC_{50}/10: 0.20 mg a.i./L	0.0175 mg a.i./L	0.0893
Diatom	Acute	Spirotetramat	96-h EC_{50}/2: 0.18 mg a.i./L	0.0175 mg a.i./L	0.0972

[1] At the screening level, the following EECs were calculated for spirotetramat (direct application):
For bees, the EEC is the maximum cumulative seasonal rate on vegetation (156 g a.i./ha, based on a half-life of 4.45 d on treated leaves). For beneficial arthropods, the EEC is the maximum cumulative rate on vegetation multiplied by a factor of 0.5 to take into consideration leaf canopy interception in orchard crops.
For earthworms, soil EEC was calculated using a maximum seasonal cumulative rate of 140 g a.i./ha (based on half-life of 0.38 d from aerobic soil biotransformation laboratory study), assuming soil bulk density of 1.5 g/cm^3 and that product is evenly distributed in the 0–15 cm soil layer.
For aquatic organisms, water EEC was calculated using a maximum cumulative seasonal rate of 140 g a.i./ha (based on half-life of 1.06 d in aerobic aquatic system).
EECs for transformation products were calculated assuming 100% conversion of spirotetramat to any of the transformation products and correcting for molecular weight.
[2] Risk Quotient (RQ) = exposure / toxicity
Shaded cells indicate that the screening level risk quotient exceeds the level of concern (LOC=1).

Table 11 Screening Level Risk Assessment on Birds and Mammals

Organism	Type of Exposure: Test Substance	Toxicity	Food Guild (Food Type)	Exposure		RQ[3]
				EEC[1]	EDE[2]	
Birds						
Bird weight: 0.02 kg	Acute: Spirotetramat	LD_{50}/10: >200 mg a.i./kg bw/d	Insectivore (small insects)	30.8 mg a.i./kg diet	7.84 mg a.i./kg bw/d	<0.0392
			Granivore (grain and seeds)	5.26 mg a.i./kg diet	1.34 mg a.i./kg bw/d	<0.0067
			Fructivore (fruit)	15.8 mg a.i./kg diet	4.04 mg a.i./kg bw/d	<0.0202
	Dietary: Spirotetramat	5-d LD_{50}/10: >49.7 mg a.i./kg bw/d	Insectivore (small insects)	30.8 mg a.i./kg diet	7.84 mg a.i./kg bw/d	<0.1651
			Granivore (grain and seeds)	5.26 mg a.i./kg diet	1.34 mg a.i./kg bw/d	<0.0283
			Fructivore (fruit)	15.8 mg a.i./kg diet	4.04 mg a.i./kg bw/d	<0.0851
	Reproduction: Spirotetramat	NOEL: 4.0 mg a.i./kg bw/d	Insectivore (small insects)	30.8 mg a.i./kg diet	7.84 mg a.i./kg bw/d	1.961
			Granivore (grain and seeds)	5.26 mg a.i./kg diet	1.34 mg a.i./kg bw/d	0.3356
			Fructivore (fruit)	15.8 mg a.i./kg diet	4.04 mg a.i./kg bw/d	1.011
Bird weight: 0.1 kg	Acute: Spirotetramat	LD_{50}/10: >200 mg a.i./kg bw/d	Insectivore (small insects)	30.8 mg a.i./kg diet	6.12 mg a.i./kg bw/d	<0.0306
			Granivore (grain and seeds)	5.26 mg a.i./kg diet	1.05 mg a.i./kg bw/d	<0.0052
			Fructivore (fruit)	15.8 mg a.i./kg diet	3.15 mg a.i./kg bw/d	<0.0158
	Dietary: Spirotetramat	5-d LD_{50}/10: >49.7 mg a.i./kg bw/d	Insectivore (small insects)	30.8 mg a.i./kg diet	6.12 mg a.i./kg bw/d	<0.1289
			Granivore (grain and seeds)	5.26 mg a.i./kg diet	1.05 mg a.i./kg bw/d	<0.0221
			Fructivore (fruit)	15.8 mg a.i./kg diet	3.15 mg a.i./kg bw/d	<0.0664
	Reproduction: Spirotetramat	NOEL: 4.0 mg a.i./kg bw/d	Insectivore (small insects)	30.8 mg a.i./kg diet	6.12 mg a.i./kg bw/d	1.530
			Granivore (grain and seeds)	5.26 mg a.i./kg diet	1.05 mg a.i./kg bw/d	0.2619
			Fructivore (fruit)	15.8 mg a.i./kg diet	3.15 mg a.i./kg bw/d	0.7887
Bird weight: 1 kg	Acute: Spirotetramat	LD_{50}/10: >200 mg a.i./kg bw/d	Insectivore (small insects)	30.8 mg a.i./kg diet	1.79 mg a.i./kg bw/d	<0.0089
			Granivore (grain and seeds)	5.26 mg a.i./kg diet	0.31 mg a.i./kg bw/d	<0.0015
			Fructivore (fruit)	15.8 mg a.i./kg diet	0.92 mg a.i./kg bw/d	<0.0046
			Herbivore (leaves, leafy crops)	192 mg a.i./kg diet	11.1 mg a.i./kg bw/d	<0.0557

Organism	Type of Exposure: Test Substance	Toxicity	Food Guild (Food Type)	Exposure		RQ[3]
				EEC[1]	EDE[2]	
	Dietary: Spirotetramat	5-d LD_{50}/10: >49.7 mg a.i./kg bw/d	Insectivore (small insects)	30.8 mg a.i./kg diet	1.79 mg a.i./kg bw/d	<0.0376
			Granivore (grain and seeds)	5.26 mg a.i./kg diet	0.31 mg a.i./kg bw/d	<0.0064
			Fructivore (fruit)	15.8 mg a.i./kg diet	0.92 mg a.i./kg bw/d	<0.0194
			Herbivore (leaves, leafy crops)	192 mg a.i./kg diet	11.1 mg a.i./kg bw/d	<0.2346
	Reproduction: Spirotetramat	NOEL: 4.0 mg a.i./kg bw/d	Insectivore (small insects)	30.8 mg a.i./kg diet	1.79 mg a.i./kg bw/d	0.4468
			Granivore (grain and seeds)	5.26 mg a.i./kg diet	0.31 mg a.i./kg bw/d	0.0765
			Fructivore (fruit)	15.8 mg a.i./kg diet	0.92 mg a.i./kg bw/d	0.2303
			Herbivore (leaves, leafy crops)	192 mg a.i./kg diet	11.1 mg a.i./kg bw/d	2.7857
Mammals						
Mammal weight: 0.015 kg	Acute: Spirotetramat	LD_{50}/10: >200 mg a.i./kg bw/d	Insectivore (small insects)	30.8 mg a.i./kg diet	4.51 mg a.i./kg bw/d	<0.0226
			Granivore (grain and seeds)	5.26 mg a.i./kg diet	0.77 mg a.i./kg bw/d	<0.0039
			Fructivore (fruit)	15.8 mg a.i./kg diet	2.33 mg a.i./kg bw/d	<0.0116
	Dietary: Spirotetramat	90-d NOEL: 148 mg a.i./kg bw/d	Insectivore (small insects)	30.8 mg a.i./kg diet	4.51 mg a.i./kg bw/d	0.0305
			Granivore (grain and seeds)	5.26 mg a.i./kg diet	0.77 mg a.i./kg bw/d	0.0052
			Fructivore (fruit)	15.8 mg a.i./kg diet	2.33 mg a.i./kg bw/d	0.0157
	Reproduction: Spirotetramat	NOEL: 71 mg a.i./kg bw/d	Insectivore (small insects)	30.8 mg a.i./kg diet	4.51 mg a.i./kg bw/d	0.0635
			Granivore (grain and seeds)	5.26 mg a.i./kg diet	0.77 mg a.i./kg bw/d	0.0109
			Fructivore (fruit)	15.8 mg a.i./kg diet	2.33 mg a.i./kg bw/d	0.0327
Mammal weight: 0.035 kg	Acute: Spirotetramat	LD_{50}/10: >200 mg a.i./kg bw/d	Insectivore (small insects)	30.8 mg a.i./kg diet	3.96 mg a.i./kg bw/d	<0.0198
			Granivore (grain and seeds)	5.26 mg a.i./kg diet	0.68 mg a.i./kg bw/d	<0.0034
			Fructivore (fruit)	15.8 mg a.i./kg diet	2.04 mg a.i./kg bw/d	<0.0102
			Herbivore (leaves, leafy crops)	192 mg a.i./kg diet	24.7 mg a.i./kg bw/d	<0.1234
	Dietary: Spirotetramat	90-d NOEL: 148 mg a.i./kg bw/d	Insectivore (small insects)	30.8 mg a.i./kg diet	3.96 mg a.i./kg bw/d	0.0267
			Granivore (grain and seeds)	5.26 mg a.i./kg diet	0.68 mg a.i./kg bw/d	0.0046

Organism	Type of Exposure: Test Substance	Toxicity	Food Guild (Food Type)	Exposure		RQ[3]
				EEC[1]	EDE[2]	
			Fructivore (fruit)	15.8 mg a.i./kg diet	2.04 mg a.i./kg bw/d	0.0138
			Herbivore (leaves, leafy crops)	192 mg a.i./kg diet	24.7 mg a.i./kg bw/d	0.1668
	Reproduction: Spirotetramat	NOEL: 71 mg a.i./kg bw/d	Insectivore (small insects)	30.8 mg a.i./kg diet	3.96 mg a.i./kg bw/d	0.0557
			Granivore (grain and seeds)	5.26 mg a.i./kg diet	0.68 mg a.i./kg bw/d	0.0095
			Fructivore (fruit)	15.8 mg a.i./kg diet	2.04 mg a.i./kg bw/d	0.0287
			Herbivore (leaves, leafy crops)	192 mg a.i./kg diet	24.7 mg a.i./kg bw/d	0.3477
Mammal weight: 1 kg	Acute: Spirotetramat	LD_{50}/10: >200 mg a.i./kg bw/d	Insectivore (small insects)	30.8 mg a.i./kg diet	2.11 mg a.i./kg bw/d	<0.0106
			Granivore (grain and seeds)	5.26 mg a.i./kg diet	0.36 mg a.i./kg bw/d	<0.0018
			Fructivore (fruit)	15.8 mg a.i./kg diet	1.09 mg a.i./kg bw/d	<0.0054
			Herbivore (leaves, leafy crops)	192 mg a.i./kg diet	13.2 mg a.i./kg bw/d	<0.0659
	Dietary: Spirotetramat	90-d NOEL: 148 mg a.i./kg bw/d	Insectivore (small insects)	30.8 mg a.i./kg diet	2.11 mg a.i./kg bw/d	0.0143
			Granivore (grain and seeds)	5.26 mg a.i./kg diet	0.36 mg a.i./kg bw/d	0.0024
			Fructivore (fruit)	15.8 mg a.i./kg diet	1.09 mg a.i./kg bw/d	0.0074
			Herbivore (leaves, leafy crops)	192 mg a.i./kg diet	13.2 mg a.i./kg bw/d	0.0890
	Reproduction: Spirotetramat	NOEL: 71 mg a.i./kg bw/d	Insectivore (small insects)	30.8 mg a.i./kg diet	2.11 mg a.i./kg bw/d	0.0298
			Granivore (grain and seeds)	5.26 mg a.i./kg diet	0.36 mg a.i./kg bw/d	0.0051
			Fructivore (fruit)	15.8 mg a.i./kg diet	1.09 mg a.i./kg bw/d	0.0153
			Herbivore (leaves, leafy crops)	192 mg a.i./kg diet	13.2 mg a.i./kg bw/d	0.1856

Organism	Type of Exposure: Test Substance	Toxicity	Food Guild (Food Type)	Exposure		RQ[3]
				EEC[1]	EDE[2]	

[1] For birds and mammals, the EEC takes into account the maximum seasonal cumulative rate on vegetation and is calculated using PMRA standard methods based on the Hoerger and Kenaga nomogram.
[2] EDE = Estimated dietary exposure; calculated for each bird or mammal size based on the EEC on appropriate food item for each food guild (at the screening level, the most conservative EEC for each food guild was used). The EDE was calculated using the following formula: (FIR/bw) × EEC. For each body weight (bw), the food ingestion rate (FIR) was based on equations from Nagy (1987). For generic birds with body weight less than or equal to 200 g, the "passerine" equation was used; for generic birds with body weight greater than 200 g, the "all birds" equation was used; for mammals, the "all mammals" equation was used:
Passerine Equation (body weight ≤200 g): FIR (g dry weight/day) = 0.398(bw in g) $^{0.850}$
All Birds Equation (body weight > 200 g): FIR (g dry weight/day) = 0.648(bw in g) $^{0.651}$
All Mammals Equation: FIR (g dry weight/day) = 0.235(bw in g) $^{0.822}$
[3] Risk Quotient (RQ) = exposure / toxicity
Shaded cells indicate that the screening level risk quotient exceeds the level of concern (LOC=1).

Table 12 Refined Risk Assessment on Non-Target Terrestrial Invertebrates and Vascular Plants

Organism	**Type of Exposure**	**Test Substance**	**Toxicity**	**Refined Exposure (Off-field EEC)[1]**	**RQ[2]**
Invertebrates					
Predatory mite	Contact	Spirotetramat 150 OD	48-h LR_{50}: 0.33 g a.i./ha	with 74% drift deposition: 57.6 g a.i./ha	174.5
				with 59% drift deposition: 45.9 g a.i./ha	139.1
				with 11% drift deposition: 8.56 g a.i./ha	25.94
Vascular plants					
Vascular plant	Vegetative vigour	Spirotetramat 150 OD	EC_{25} (corn): 76 g a.i./ha	with 74% drift deposition: 115 g a.i./ha	1.5155
				with 59% drift deposition: 91.8 g a.i./ha	1.2083
				with 11% drift deposition: 17.1 g a.i./ha	0.2253

[1] 74% spray deposition: early season spray drift at one metre downwind resulting from airblast applications
59% spray deposition: late season spray drift at one metre downwind resulting from airblast applications
11% spray deposition: spray drift deposition at one metre downwind resulting from groundboom application with a fine droplet spray quality (ASAE fine classification)
[2] Risk Quotient (RQ) = exposure / toxicity
Shaded cells indicate that the screening level risk quotient exceeds the level of concern (LOC=1).

Table 13 Refined Risk Assessment on Birds

Organism	Type of Exposure: Test Substance	Toxicity	Food Guild (Food Type)	Refined Exposure		RQ[2]
				EEC	EDE[1]	
Bird weight: 0.02 kg	Reproduction: Spirotetramat	NOEL: 4.0 mg a.i./kg bw/d	Insectivore (small insects)	Off-field assessment		
				30.8 mg a.i./ kg diet	with 74% drift deposition: 5.80 mg a.i./kg bw/d	1.451
					with 59% drift deposition: 4.63 mg a.i./kg bw/d	1.157
					with 11% drift deposition: 0.86 mg a.i./kg bw/d	0.2157
			Fructivore (fruit)	Off-field assessment		
				15.8 mg a.i./kg diet	with 74% drift deposition: 2.99 mg a.i./kg bw/d	0.7479
Bird weight: 0.1 kg	Reproduction: Spirotetramat	NOEL: 4.0 mg a.i./kg bw/d	Insectivore (small insects)	Off-field assessment		
				30.8 mg a.i./ kg diet	with 74% drift deposition: 4.53 mg a.i./kg bw/d	1.132
					with 59% drift deposition: 3.61 mg a.i./kg bw/d	0.9029
			Insectivore (large insects—additional food type)	In-field assessment		
				5.26 mg a.i./kg diet	1.05 mg a.i./kg bw/d	0.2619

Bird weight: 1 kg	Reproduction: Spirotetramat	NOEL: 4.0 mg a.i./kg bw/d	Herbivore (leaves, leafy crops)	Off-field assessment		
				192 mg a.i./kg diet	with 74% drift deposition: 8.25 mg a.i./kg bw/d	2.0615
					with 59% drift deposition: 6.57 mg a.i./kg bw/d	1.6436
					with 11% drift deposition: 1.23 mg a.i./kg bw/d	0.3064
			Herbivore (short grass—additional food type)	In-field assessment		
				110 mg a.i./kg diet	6.39 mg a.i./kg bw/d	1.598
				Different food type than at screening level; off-field assessment		
				110 mg a.i./kg diet	with 74% drift deposition: 4.72 mg a.i./kg bw/d	1.180
					with 59% drift deposition: 3.77 mg a.i./kg bw/d	0.9425
			Herbivore (long grass—additional food type)	In-field assessment		
				67.1 mg a.i./kg diet	3.89 mg a.i./kg bw/d	0.9725

[1] EDE = Estimated dietary exposure; calculated for each bird size based on the EEC on appropriate food item for each food guild. For the refined assessment, the EEC was based on an off-field scenario and considered additional food types. For off-field EECs, the following deposition rates were used:
74% spray deposition: early season spray drift at one metre downwind resulting from airblast applications
59% spray deposition: late season spray drift at one metre downwind resulting from airblast applications
11% spray deposition: spray drift deposition at one metre downwind resulting from groundboom application with a fine droplet spray quality (ASAE fine classification)
The EDE was calculated using the following formula: (FIR/bw) × EEC. For each body weight (bw), the food ingestion rate (FIR) was based on equations from Nagy (1987). For generic birds with body weight less than or equal to 200 g, the "passerine" equation was used; for generic birds with body weight greater than 200 g, the "all birds" equation was used:
Passerine Equation (body weight ≤ 200 g): FIR (g dry weight/day) = $0.398(\text{bw in g})^{0.850}$
All Birds Equation (body weight > 200 g): FIR (g dry weight/day) = $0.648(\text{bw in g})^{0.651}$
[2] Risk Quotient (RQ) = exposure / toxicity
Shaded cells indicate that the risk quotient exceeds the level of concern (LOC=1).

Table 14 Alternative Active Ingredients for Movento 150 OD Insecticide and Movento 240 SC Insecticide

Crop	Pest	Alternative
Grapes	Phylloxera	Endosulfan, malathion
	Mealybug	Diazinon, malathion, potassium salt of fatty acid
	Scale	Potassium salt of fatty acid, malathion
	Whitefly	Permethrin (ornamental grape)
Pears	Pear psylla	Mancozeb, diazinon, endosulfan, malathion, phosalone, dimethoate, azinphos-methyl, phosmet, carbaryl, deltamethrin, cypermethrin, permethrin, lambda-cyhalothrin, pyridaben, amitraz, abamectin, thiamethoxam, potassium salt of fatty acid, kaolin, oil
Apples	Scale	Diazinon, carbaryl, azinphos-methyl, phosmet, malathion, pyrethrins, lime sulphur, oil
	Aphid	Diazinon, endosulfan, phosmet, methomyl, phosalone, pirimicarb, oxamyl, delatmethrin, lambda-cyhalothrin, imidacloprid, thiamethoxam,
	Whiteflies	None
	Mealybug	Malathion, carbaryl, azinphos-methyl, pyrethrin
Peaches	Aphid	Diazinion, endosulfan, malathion, dimethoate, pirimicarb, imidacloprid, lambda-cyhalothrin
	Whitefly	None
	Mealybug	None
	Scale	Diazinon, carbaryl, azinphos-methyl, potassium salt of fatty acid, oil, calcium polysulphide
Nuts	Aphid	Acetamiprid (non-bearing), dimethoate, chlorpyrifos, potassium salt of fatty acid
	Mealybug	Acetamiprid (non-bearing), potassium salt of fatty acid
	Scale	Potassium salt of fatty acid
	Whiteflies	Acetamiprid (non-bearing), potassium salt of fatty acids
	Phylloxera	N/A
Hops	Hop aphid	N/A
Cucurbits	Aphids	Malathion, pyrethrins, endosulfan, diazinon,
	Whiteflies	Spiromesifen
Fruiting Vegetables	Aphids	Malathion, endosulfan, pyrethrins, methomyl, acephate, diazinon, dimethoate,
	Whiteflies	Spiromesifen
	Psyllids	N/A
Leafy Vegetables - non *Brassica*	Aphids	Malathion, endosulfan, pyrethrins, naled, acephate, diazinon, dimethoate, imidacloprid,
	Whiteflies	Spiromesifen
Leafy Vegetables - *Brassica*	Aphids	Malathion, endosulfan, pyrethrins, naled, acephate, diazinon, dimethoate, imidacloprid,
	Whiteflies	Spiromesifen
Tuberous and corm vegetables	Aphids	Endosulfan, pyrethrins, deltamethrin, methomyl, acephate, diazinon, dimethoate, imidacloprid,
	Psyllids	N/A
	Whiteflies	Spiromesifen

Table 15 Use (label) Claims Proposed by Applicant and Whether Acceptable or Unsupported

Applicant proposed label claims	Accepted label claims	Unsupported label claims
Control of mealybugs, phylloxera and whiteflies, and suppression of Lecanium scale and spider mites on grape and small fruit vine climbing (Crop Subgroup 13F)	Control of mealybugs, whiteflies and phylloxera, and suppression of Lecanium scale on grape (excluding table grapes) and small fruit vine climbing (Crop Subgroup 13F)	Spider mites
Control of aphids, whiteflies, mealybugs, pear psylla and San Jose scale, and suppression of micro-lepidoptera leafminers, rust mites, spider mites and white apple leafhopper on pome fruit (Crop Group 11)	Control of rosy apple aphid, apple aphids, whiteflies, pear psylla, mealybugs and San Jose scale on pome fruit (Crop Group 11)	Micro-Lepidoptera leafminers, rust mites, spider mites and white apple leafhopper
Control of aphids, whiteflies, mealybugs, San Jose scale and white peach scale, and suppression of black scale, cherry fruit flies, Lecanium scale, rust mites, spider mites	Control of aphids, whiteflies, mealybugs, San Jose scale and white peach scale, and suppression of Lecanium scale on stone fruit (Crop Group 12)	Cherry fruit flies, rust mites and spider mites and black scale
Control of aphids, phylloxera, whiteflies, mealybugs, San Jose scale, walnut scale, and suppression of Lecanium scale, olive scale and spider mites on tree nuts (Crop Group 14)	Control of aphids, phylloxera, whiteflies, mealybugs, San Jose scale and walnut scale, and suppression of Lecanium scale on tree nuts (Crop Group 14)	Olive scale and spider mites
Control of hop aphid and suppression of spider mites on hops	Control of hop aphid on hops	Spider mites
Control of aphids (including root aphids and adelgids) and scales and suppression of rust mites and spider mites on Christmas trees	N/A	Control of aphids (including root aphids and adelgids) and scales, and suppression of rust mites and spider mites on Christmas trees
Control of aphids and whiteflies and suppression of spider mites on cucurbit vegetables (Crop Group 9)	Control of aphids and whiteflies on cucurbit vegetables (Crop Group 9)	Spider mites
Control of aphids, psyllids and whiteflies, and suppression of broad mite, russet mite, and spider mite on fruiting vegetables (Crop Group 8)	Control of aphids, psyllids and whiteflies on fruiting vegetables (Crop Group 8)	Broad mite, russet mite and spider mite
Control of aphids and whiteflies and suppression of diamondback moth on non-*Brassica* leafy vegetables (Crop Group 4)	Control of aphids and whiteflies on non-*Brassica* leafy vegetables (Crop Group 4)	Diamondback moth
Control of aphids and whiteflies and suppression of diamondback moth on *Brassica* leafy vegetables (Crop Group 5)	Control of aphids and whiteflies on *Brassica* leafy vegetables (Crop Group 5)	Diamondback moth

Applicant proposed label claims	Accepted label claims	Unsupported label claims
Control of aphids, psyllids and whiteflies, and suppression of spider mites and potato tuberworm on tuberous and corm vegetables (Crop Subgroup 1C)	Control of aphids, psyllids and whiteflies on tuberous and corm vegetables (Crop Subgroup 1C)	Spider mites and potato tuberworm

Appendix II Supplemental Maximum Residue Limit Information—International Situation and Trade Implications

All of the specified Canadian MRLs are the same as those in the U.S. There are no Codex MRLs established at this time.

Appendix III Crop Groups: Numbers and Definitions

Crop Group	Name of the Crop Group	Food Commodities Included in the Crop Group
1C	Root and tuber vegetables, Tuberous and corm vegetables subgroup	Arracacha Arrowroot Cassava roots Chayote roots Chinese artichokes Chufa Edible canna Ginger roots Jerusalem artichokes Lerens Potatoes Sweet potato roots Tanier corm Taro corm True yam tubers Turmeric roots Yam bean roots
4	Leafy vegetables (except *Brassica* Vegetables)	Amaranth Arugula Cardoon Celery Celtuce Chinese celery Corn salad Dandelion leaves Dock Edible leaved chrysanthemum Endives Fresh chervil leaves Fresh Florence fennel leaves and stalk Fresh parsley leaves Garden cress Garden purslane Garland chrysanthemum Head lettuce Leaf lettuce New Zealand spinach Orach leaves Radicchio Rhubarb Spinach Swiss chard Upland cress Vine spinach Winter purslane

Crop Group	Name of the Crop Group	Food Commodities Included in the Crop Group
5A	*Brassica* (cole) leafy vegetables, Head and stem *Brassica* subgroup	Broccoli Brussels sprouts Cabbage Cauliflower Chinese broccoli Chinese mustard cabbage Kohlrabi Napa Chinese cabbage
5B	*Brassica* (cole) leafy vegetables, Leafy *Brassica* greens subgroup	Bok choy Chinese cabbage Broccoli raab Collards Kale Mustard greens Mustard spinach Rape greens
8	Fruiting vegetables	Bell peppers Eggplants Groundcherries Non-bell peppers Pepinos Pepper hybrids Tomatillos Tomatoes
9	Cucurbit vegetables	Balsam apples Balsam pears Cantaloupes Chayote fruit Chinese cucumbers Chinese waxgourds Citron melons Cucumbers Edible gourds (other than those listed in this item) Muskmelons (other than those listed in this item) Pumpkins Summer squash Watermelons West Indian gherkins Winter squash
10	Citrus fruits	Calamondins Citrus citron Citrus hybrids Grapefruits Kumquats Lemons Limes Oranges Pummelos Satsuma mandarins Tangerines

Crop Group	Name of the Crop Group	Food Commodities Included in the Crop Group
11	Pome fruits	Apples Crabapples Loquats Mayhaws Oriental pears Pears Quinces
12	Stone fruits	Apricots Nectarines Peaches Plumcots Plums Prune plums Sweet cherries Tart cherries
13-07F	Small fruit vine climbing, except fuzzy kiwifruit	Amur river grape Gooseberry Grape Hardy kiwifruit Maypop Schisandra berry
14	Tree nuts	Almonds Beechnuts Black walnuts Brazil nuts Butternuts Cashews Chestnuts Chinquapins English walnuts Filberts Hickory nuts Macadamia nuts Pecans Pistachios Walnuts (other than those listed in this item)

References

A. LIST OF STUDIES/INFORMATION SUBMITTED BY REGISTRANT

Chemistry

Spirotetramat Technical Insecticide

PMRA Document Number	Reference
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1314119	2003, BYI 08330 (AE 1302943) - Physical characteristics color, appearance and odor, PA03/035, DACO: 2.14.1,2.14.3
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Movento® 240 SC Insecticide

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1314449	2006, Independent laboratory validation of analytical method 00836 for the determination of BYI 08330 and BYI 08330-enol in drinking and surface water by HPLC-MS/MS and HPLC-UV, RAFNX019, MRID: 469044-93, DACO: 3.7,5.14,7.8,8.6
1314549	2006, Tier 2 summary of the identity of the plant protection product for Spirotetramat (BYI 08330) OD 150, M-275699-01-1, DACO: 3.7
1314550	2006, Tier 2 summary of the physical, chemical and technical properties of the plant protection product for Spirotetramat (BYI 08330) OD 150, M-275702-01-1, DACO: 3.5
1314611	2006, Reference list of the physical, chemical and technical properties of on the plant protection product Spirotetramat 150 g/L OD Material No.: 06424376 sorted by Annex points, M-277289-01-1, DACO: 3.5.1,3.5.2,3.5.3
1314615	2006, Product chemistry of Movento 150 OD insecticide, BR2531, MRID: 469044-03C, DACO: 3.0 CBI
1314620	2006, Independent laboratory validation of method FN-002-S05-02 for the determination of BYI08330 and its metabolites BYI08330-enol, BYI08330-keto-hydroxy and BYI08330-MA-amide in soil and sediment by LC/MS/MS, MR-06/037, MRID: 469044-15, DACO: 3.7,5.14
1314740	2006, Tier 2 summary of the identity of the plant protection product for Spirotetramat (BYI 08330) OD 150 - Confidential information, M-275693-02-1, DACO: 3.7 CBI
1314777	2006, Tier 2 summary of the identity of the plant protection product for Spirotetramat (BYI 08330) OD 150, M-275699-01-1, DACO: 3.7
1314778	2006, Tier 2 summary of the physical, chemical and technical properties of the plant protection product for Spirotetramat (BYI 08330) OD 150, M-275702-01-1, DACO: 3.7
1314803	2006, Reference list of the physical, chemical and technical properties of on the plant protection product Spirotetramat 150 g/L OD Material No.: 06424376 sorted by Annex points, M-277289-01-1, DACO: 3.5.1,3.5.2,3.5.3

2.0 Impact on Human and Animal Health

PMRA Document Number	Reference
1314092	2004, An acute oral LD50 study in the rat with BYI 08330, 200398, MRID: 469045-27, DACO: 4.2.1
1314138	2005, Technical grade BYI 08330: A subchronic toxicity testing study in the rat, 201136, MRID: 469045-38, DACO: 4.3.1
1314139	2004, Technical grade BYI 08330: A subacute toxicity feeding study in the Beagle dog, 201012, MRID: 469045-72, DACO: 4.3.3
1314154	2005, Technical grade BYI 08330 - A 90-day subchronic toxicity feeding study in the Beagle dog, 201223, MRID: 469045-41, DACO: 4.3.2
1314156	2005, An acute oral neurotoxicity screening study with technical grade BYI 08330 in Wistar Rats, 201283, MRID: 469045-60, DACO: 4.5.12
1314160	2006, BYI 08330-mono-hydroxy (Project: BYI 08330) - Salmonella/microsome test - Plate incorporation and preincubation method, AT02716, MRID: 469046-04, DACO: 4.8
1314161	2006, BYI 08330 150 OD - Acute skin irritation/corrosion on rabbits, AT02359, MRID: 469045-80, DACO: 4.6.5
1314162	2006, Chromosome aberration assay in bone marrow cells of the mouse with BYI 08330, AR00070, MRID: 469045-58, DACO: 4.5.7
1314185	2006, BYI 08330 - Study for the skin sensitization effect in guinea pigs (guinea pig maximization test according to Magnusson and Kligman), 32273, MRID: 469045-33, DACO: 4.2.6
1314211	2005, Acute eye irritation study of BYI 08330 by instillation into the conjunctival sac of rabbits, R8146, MRID: 469045-31, DACO: 4.2.4
1314212	2006, BYI 08330 150 OD - Acute eye irritation on rabbits, AT02358, MRID: 469045-79, DACO: 4.6.4
1314213	2002, Acute skin irritation test (patch test) of BYI 8330 in rabbits, R8147, MRID: 469045-32, DACO: 4.2.5
1314214	2002, BYI 08330 - Micronucleus-test on the male mouse, AT00048, MRID: 469045-56, DACO: 4.5.7
1314215	2003, BYI 08330 - Unscheduled DNA synthesis test with rat liver cells in vivo, AT00526, MRID: 469045-57, DACO: 4.5.8
1314216	2004, BYI 08330 - Study for the skin sensitization effect in guinea pigs (Buehler Patch test), AT01317, MRID: 469045-34, DACO: 4.2.6
1314217	2002, BYI 08330 - Salmonella/microsome test plate incorporation and preincubation method, AT00056, MRID: 469045-52, DACO: 4.5.4
1314218	2005, BYI 08330 150 OD (Project: BYI 08330) - Study for the skin sensitization effect in guinea pigs (Buehler patch test), AT01873, MRID: 469045-82, DACO: 4.6.6
1314219	2005, BYI 08330 150 OD - Acute toxicity in the rat after oral administration, AT02161, MRID: 469045-76, DACO: 4.6.1

1314220	2005, BYI 08330 240 SC - Acute toxicity in the rat after oral administration, AT02162, MRID: 469045-85, DACO: 4.6.1
1314221	2005, BYI 08330 150 OD - Acute toxicity in the rat after dermal application, AT02164, MRID: 469045-77, DACO: 4.6.2
1314222	2005, BYI 08330 240 SC - Acute toxicity in the rat after dermal application, AT02165, MRID: 469045-86, DACO: 4.6.2
1314223	2005, BYI 08330 240 SC - Acute eye irritation on rabbits, AT02290, MRID: 469045-88, DACO: 4.6.4
1314225	2004, BYI 08330 - Developmental toxicity study in rabbits after oral administration, AT01003 (Study No. T 3063167), MRID: 469045-44, DACO: 4.5.3
1314228	2004, An acute dermal LD50 study in the rat with BYI 08330, 200399, MRID: 469045-29, DACO: 4.2.2
1314245	2005, Technical grade BYI 08330 (common name Spirotetramat): a chronic toxicity testing study in the rat, 201285, MRID: 469045-47, DACO: 4.4.1
1314272	2005, BYI 08330, Synonym: FHN 08330 - Developmental toxicity study in rats after oral administration, AT01413, MRID: 469045-43, DACO: 4.5.2
1314278	2006, BYI 08330 240 SC - Acute skin irritation/corrosion on rabbits, AT02291, MRID: 469045-89, DACO: 4.6.5
1314279	2006, BYI 08330 - Synonym: FHN 08330 - Supplementary developmental toxicity study in rats after oral administration, AT01512, MRID: 469045-45, DACO: 4.5.2
1314281	2006, BYI 08330 240 SC (Project: BYI 08330) - Study for the skin sensitization effect in guinea pigs (Buehler patch test), AT01876, MRID: 469045-90, DACO: 4.6.6
1314282	2006, BYI 08330 150 OD - Acute inhalation toxicity in rats, AT02396, MRID: 469045-78, DACO: 4.6.3
1314283	2006, BYI 08330-CIS-Ketohydroxy - Acute toxicity in the rat after oral administration, AT02506, MRID: 469045-93, DACO: 4.6.1
1314284	2006, BYI 08330 150 OD ready to use dilution (Project: BYI 08330) - Study for the skin sensitization effect in guinea pigs (Buehler patch test), AT02570, MRID: 469045-81, DACO: 4.6.6
1314285	2006, BYI 08330-desmethyl-ketohydroxy - Acute toxicity in the rat after oral administration, AT02927, MRID: 469045-96, DACO: 4.6.1
1314291	2006, [Azaspirodecenyl-3-14C]BYI 08330: Distribution of the total radioactivity in male and female rats determined by quantitative whole body autoradiography (QWBA) including determination of the total radioactivity in excreta and exhaled 14CO2, MEF-06/15
1314294	2006, BYI 08330 - Evaluation of potential dermal sensitization in the local lymph node assay, SA 04120, MRID: 469045-65, DACO: 4.2.6
1314296	2006, BYI 08330 240 SC ready to use dilution (Project: BYI 08330) - Study for the skin sensitization effect in guinea pigs (Buehler patch test), AT02598, MRID: 469045-91, DACO: 4.6.6
1314297	2006, BYI 08330 240 SC - Acute inhalation toxicity in rats, AT02374, MRID: 469045-87, DACO: 4.6.3

1314311	2006, [Azaspirodecenyl-3-14C]BYI 08330-enol-glucoside supplemental study: adsorption, distribution, excretion and metabolism in the rat, MEF-06/006, MRID: 469046-02, DACO: 4.5.9
1314318	2006, BYI 08330 - Cytogenetic screening with chinese hamster V79 cells, AT00194, MRID: 469045-55, DACO: 4.5.6
1314327	2006, Technical grade BYI 08330 (common name Spirotetramat): An oncogenicity testing study in the rat, 201358, MRID: 469045-49, DACO: 4.4.2
1314329	2006, BYI 08330-desmethyl-ketohydroxy (Project: BYI 08330) - Salmonella/microsome test - Plate incorporation and preincubation method, AT03027, MRID: 469045-97, DACO: 4.8
1314330	2006, BYI 08330-di-hydroxy (Project: BYI 08330) - Salmonella/microsome test - Plate incorporation and preincubation method, AT03069, MRID: 469045-99, DACO: 4.8
1314331	2006, BYI 08330 - Salmonella/microsome test - Plate incorporation and preincubation method, AT03070, MRID: 469045-51, DACO: 4.5.4
1314337	2006, BYI 08330-Enol - Investigation of the testicular/sperm toxicity in the rat following 21 days of exposure by gavage, SA06011, DACO: 4.8
1314341	2006, BYI 08330 - In vitro chromosome aberration test with chinese hamster V79 cells, AT00055, MRID: 469045-54, DACO: 4.5.6
1314367	2005, Technical grade BYI 08330: A subchronic toxicity testing study in the mouse, 201284, MRID: 469045-39, DACO: 4.3.1
1314378	G.D. Cappon, T.L. Fleeman, R.E. Chapin, and M.E. Hurtt, 2005, Effects of feed restriction during organogenesis on embryo-fetal development in rabbit, Birth Defects Research Part B: Developmental and Reproductive Toxicology: 44(5) 424-430. DACO: 4.4.5
1314381	2006, Validation of the Buehler Patch Test Mehod used by the Health Care Toxicology of Bayer HealthCareAG, performed in guinea pigs of the strain Crl:HA with Alpha Hexyl Cinnamic Aldehyde, AT01212, MRID: 469045-35, DACO: 4.6.6
1314382	2006, BYI 08330 - V79/HPRT-test in vitro for the detection of induced forward mutations, AT00137A, MRID: 469045-53, DACO: 4.5.5
1314413	2005, A homogeneity and stability study of BYI 08330 technical in rodent ration, 201297, MRID: 469045-73, DACO: 4.6.8,4.7.7,5.14
1314422	2004, A liquid chromatographic method for the determination of BYI 08330 in rodent ration, 200423, MRID: 469045-75, DACO: 4.6.8,4.7.7,5.14
1314427	2006, BYI 08330-di-hydroxy - Acute toxicity in the rat after oral administration, AT02995, MRID: 469045-98, DACO: 4.2.9
1314428	2006, A chronic toxicity feeding study in the beagle dog with technical grade BYI 08330, 201486, MRID: 469045-48, DACO: 4.3.2
1314433	2006, BYI 08330 (Spirotetramat) - Assessment of literature research in various databases, M-275046-01-1, DACO: 4.8
1314438	2006, BYI 08330 - Pilot study on developmental toxicity in rats after oral administration, T3068559, MRID: 469045-59, DACO: 4.5.2
1314466	2006, A subacute dermal toxicity study in rats with BYI 08330, 201505, MRID: 469045-42, DACO: 4.3.5

1314474	2006, BYI 08330-mono-hydroxy - Acute toxicity in the rat after oral administration, AT02687, MRID: 469046-03, DACO: 4.2.9
1314476	2006, BYI 08330 - Evaluation of the potential reproductive toxicity in the male rat following daily oral administration by gavage, SA 04181, MRID: 469045-69, DACO: 4.8
1314542	2006, Technical grade BYI 08330 (common name Spirotetramat): A two generation reproductive toxicity study in the Wistar rat, 201426-1, MRID: 469045-46, DACO: 4.5.1
1314554	2006, Cyclic ketoenols BSN 3457, BSN 2342, FHN 7504, FHN 8330 - Subacute exploratory toxicity studies in rats (application by feed over 4 weeks), T0061869, MRID: 469045-37, DACO: 4.3.3
1314555	2006, Technical grade BY1 08330 - A dose range-finding reproductive toxicity study in the Wistar rat (revised report), 201300-1, MRID: 469045-71, DACO: 4.5.1
1314557	2006, BYI 08330 (c.n.: --) - Study on acute inhalation toxicity in rats according to OECD no. 403, 32020, MRID: 469045-30, DACO: 4.2.3
1314558	2006, Physiology based pharmacokinetic simulation of BYI 08330 in male rats, BTS-WSM0602, MRID: 469045-67, DACO: 4.5.9
1314560	2006, BYI 08330-Enol: Exploratory 10-day toxicity study in the rat by gavage, M-274171-01-2, MRID: 469046-01, DACO: 4.3.8
1314563	2006, BYI 08330 - Pilot developmental toxicity study in rabbits after oral administration, T3062735, MRID: 469045-70, DACO: 4.5.3
1314584	2006, BYI 08330 - Subacute study with mice (keto-enol design), T2070951, MRID: 469045-36, DACO: 4.3.3
1314585	2006, [Azaspirodecenyl-3-14C]-BYI 08330: Comparison of the in vitro metabolism in liverbeads from male rat, mouse and human, SA05319, MRID: 469045-66, DACO: 4.5.9
1314632	2006, [Azaspirodecane-3-14C]BYI 08330-ketohydroxy: Adsorption, distribution, excretion and metabolism in the rat, MEF-06/007, MRID: 469045-95, DACO: 4.5.9
1314635	2006, PBPK-Simulation of BYI 08330 in male rats at high doses, BTS-WSM0603-1, MRID: 469045-68, DACO: 4.5.9
1314686	2006, Tier 1 summary of the toxicological studies and exposure data and information on the plant protection product Spirotetramat 150 g/L OD - Material No.: 06424376, M-277320-03-1, DACO: 4.1,5.1
1314691	2006, [Azaspirodecenyl-3-14C]BYI 08330: Adsorption, distribution, excretion and metabolism in the rat, MEF-048/04, MRID: 469045-04, DACO: 4.5.9
1314693	2006, Tier 2 summary of the toxicological and toxicokinetic studies on the active substance for Spirotetramat (BYI 08330), M-277720-02-1, DACO: 4.1
1314717	2006, Tier 2 summary of the toxicological studies and exposure data and information on the plant protection product Spirotetramat 150 g/L OD , material no. 06424376, M-278141-01-1, DACO: 4.1,5.1
1314718	2006, Tier 2 summary of the toxicological studies and exposure data and information on the plant protection product for Spirotetramat 240 SC - Material No. 06 424 384, M-278143-01-1, DACO: 4.1,5.1

1314721	2006, Revised report : Technical grade BYI 08330 (common name Spirotetramat): An oncogenicity testing study in the mouse, 201359-1, MRID: 469045-50, DACO: 4.4.3
1314723	2005, A revised homogeneity and stability study of BYI 08330 technical in rodent ration, 201363, MRID: 469045-74, DACO: 4.4.3
1314725	2006, Tier 1 summary of the toxicological and toxicokinetic studies on the active substance - Spirotetramat (BYI08330), M-277522-03-1, DACO: 4.1
1314738	2005, Technical grade BYI 08330 (common name Spirotetramat): a chronic toxicity testing study in the rat, 201285, MRID: 469045-47, DACO: 4.4.1
1314831	2006, Tier 1 summary of the toxicological studies and exposure data and information on the plant protection product Spirotetramat 150 g/L OD - Material No.: 06424376, M-277320-03-1, DACO: 4.1
1314833	2006, Tier 2 summary of the toxicological and toxicokinetic studies on the active substance for Spirotetramat (BYI 08330), M-277720-02-1, DACO: 4.1
1314846	2006, Tier 2 summary of the toxicological studies and exposure data and information on the plant protection product Spirotetramat 150 g/L OD , material no. 06424376, M-278141-01-1, DACO: 4.1,5.1
1314847	2006, Tier 2 summary of the toxicological studies and exposure data and information on the plant protection product for Spirotetramat 240 SC - Material No. 06 424 384, M-278143-01-1, DACO: 4.1,5.1
1314851	2006, Tier 1 summary of the toxicological and toxicokinetic studies on the active substance - Spirotetramat (BYI08330), M-277522-03-1, DACO: 4.1
1314220	2005, BYI 08330 240 SC - Acute toxicity in the rat after oral administration, AT02162, MRID: 469045-85, DACO: 4.6.1
1314222	2005, BYI 08330 240 SC - Acute toxicity in the rat after dermal application, AT02165, MRID: 469045-86, DACO: 4.6.2
1314223	2005, BYI 08330 240 SC - Acute eye irritation on rabbits, AT02290, MRID: 469045-88, DACO: 4.6.4
1314278	2006, BYI 08330 240 SC - Acute skin irritation/corrosion on rabbits, AT02291, MRID: 469045-89, DACO: 4.6.5
1314281	2006, BYI 08330 240 SC (Project: BYI 08330) - Study for the skin sensitization effect in guinea pigs (Buehler patch test), AT01876, MRID: 469045-90, DACO: 4.6.6
1314296	2006, BYI 08330 240 SC ready to use dilution (Project: BYI 08330) - Study for the skin sensitization effect in guinea pigs (Buehler patch test), AT02598, MRID: 469045-91, DACO: 4.6.6
1314297	2006, BYI 08330 240 SC - Acute inhalation toxicity in rats, AT02374, MRID: 469045-87, DACO: 4.6.3
1314686	2006, Tier 1 summary of the toxicological studies and exposure data and information on the plant protection product Spirotetramat 150 g/L OD - Material No.: 06424376, M-277320-03-1, DACO: 4.1,5.1
1314717	2006, Tier 2 summary of the toxicological studies and exposure data and information on the plant protection product Spirotetramat 150 g/L OD , material no. 06424376, M-278141-01-1, DACO: 4.1,5.1

1314718	2006, Tier 2 summary of the toxicological studies and exposure data and information on the plant protection product for Spirotetramat 240 SC - Material No. 06 424 384, M-278143-01-1, DACO: 4.1,5.1
1314831	2006, Tier 1 summary of the toxicological studies and exposure data and information on the plant protection product Spirotetramat 150 g/L OD - Material No.: 06424376, M-277320-03-1, DACO: 4.1
1314846	2006, Tier 2 summary of the toxicological studies and exposure data and information on the plant protection product Spirotetramat 150 g/L OD , material no. 06424376, M-278141-01-1, DACO: 4.1,5.1
1314847	2006, Tier 2 summary of the toxicological studies and exposure data and information on the plant protection product for Spirotetramat 240 SC - Material No. 06 424 384, M-278143-01-1, DACO: 4.1,5.1
1314161	2006, BYI 08330 150 OD - Acute skin irritation/corrosion on rabbits, AT02359, MRID: 469045-80, DACO: 4.6.5
1314212	2006, BYI 08330 150 OD - Acute eye irritation on rabbits, AT02358, MRID: 469045-79, DACO: 4.6.4
1314218	2005, BYI 08330 150 OD (Project: BYI 08330) - Study for the skin sensitization effect in guinea pigs (Buehler patch test), AT01873, MRID: 469045-82, DACO: 4.6.6
1314219	2005, BYI 08330 150 OD - Acute toxicity in the rat after oral administration, AT02161, MRID: 469045-76, DACO: 4.6.1
1314221	2005, BYI 08330 150 OD - Acute toxicity in the rat after dermal application, AT02164, MRID: 469045-77, DACO: 4.6.2
1314282	2006, BYI 08330 150 OD - Acute inhalation toxicity in rats, AT02396, MRID: 469045-78, DACO: 4.6.3
1314284	2006, BYI 08330 150 OD ready to use dilution (Project: BYI 08330) - Study for the skin sensitization effect in guinea pigs (Buehler patch test), AT02570, MRID: 469045-81, DACO: 4.6.6
1314686	2006, Tier 1 summary of the toxicological studies and exposure data and information on the plant protection product Spirotetramat 150 g/L OD - Material No.: 06424376, M-277320-03-1, DACO: 4.1,5.1
1314717	2006, Tier 2 summary of the toxicological studies and exposure data and information on the plant protection product Spirotetramat 150 g/L OD , material no. 06424376, M-278141-01-1, DACO: 4.1,5.1
1314725	2006, Tier 1 summary of the toxicological and toxicokinetic studies on the active substance - Spirotetramat (BYI08330), M-277522-03-1, DACO: 4.1
1314831	2006, Tier 1 summary of the toxicological studies and exposure data and information on the plant protection product Spirotetramat 150 g/L OD - Material No.: 06424376, M-277320-03-1, DACO: 4.1
1314846	2006, Tier 2 summary of the toxicological studies and exposure data and information on the plant protection product Spirotetramat 150 g/L OD , material no. 06424376, M-278141-01-1, DACO: 4.1,5.1
1314851	2006, Tier 1 summary of the toxicological and toxicokinetic studies on the active substance - Spirotetramat (BYI08330), M-277522-03-1, DACO: 4.1
1314123	2004, Degradation of [azaspirodecenyl-3-^{14}C]BYI08330 by plant suspension cell

	cultures (supplemental study to metabolism in plants), MEF-262/03 (and Study No. M1711274-3), DACO: 6.3
1314182	2006, Enforcement method 00888 for the determination of residues of BYI 08330 and BYI08330-enol in/on plant material by HPLC-MS/MS, MR-102/04 (and Method No. 00888), DACO: 7.2.1,7.2.4
1314184	2006, Metabolism of [azaspirodecenyl-3-^{14}C]BYI08330 in lettuce, MEF-049/04 (and Study No. M1731301-6), MRID: 469044-81, DACO: 6.3
1314229	2006, Independent laboratory validation of BCS analytical method 00969 for the determination of residues of BYI08330-enol in materials of animal origin, P613060584 (and Report No. P/B 964 G), DACO: 7.2.1,7.2.4
1314230	2006, Independent laboratory validation of BCS analytical method 00888 for the determination of residues of BYI08330 and BYI08330-enol in plant material, P612060583 (and Study No. P 965 G), DACO: 7.2.1,7.2.4
1314288	2006, Metabolism of [azaspirodecenyl-3-^{14}C]BYI 08330 in the laying hen, MEF-05/273 (and Study No. M81819135), MRID: 469044-83, DACO: 6.2
1314289	2006, [Azaspirodecenyl-3-14C]BYI 08330: Absorption, distribution, excretion, and metabolism in the lactating goat, MEF-05/293 (and Study No. M31819130), MRID: 469044-82, DACO: 6.2
1314290	2006, Metabolism of [azaspirodecenyl-3-^{14}C]BYI 08330 in potatoes, MEF-05/320 (and Study No. M1731386-9), MRID: 469044-84, DACO: 6.3
1314293	2006, Metabolism of [azaspirodecenyl-3-^{14}C]BYI 08330 in cotton after spray application, MEF-236/04 (and Study No. M1731275-6), MRID: 469044-79, DACO: 6.3
1314288	2006, Metabolism of [azaspirodecenyl-3-^{14}C]BYI 08330 in the laying hen, MEF-05/273 (and Study No. M81819135), MRID: 469044-83, DACO: 6.2
1314289	2006, [Azaspirodecenyl-3-^{14}C]BYI 08330: Absorption, distribution, excretion, and metabolism in the lactating goat, MEF-05/293 (and Study No. M31819130), MRID: 469044-82, DACO: 6.2
1314290	2006, Metabolism of [azaspirodecenyl-3-^{14}C]BYI 08330 in potatoes, MEF-05/320 (and Study No. M1731386-9), MRID: 469044-84, DACO: 6.3
1314293	2006, Metabolism of [azaspirodecenyl-3-^{14}C]BYI 08330 in cotton after spray application, MEF-236/04 (and Study No. M1731275-6), MRID: 469044-79, DACO: 6.3
1314310	2005, [Azaspirodecenyl-2-^{14}C]BYI08330: Extraction efficiency testing of the residue method for the determination of BYI08330, BYI08330-enol, BYI08330-ketohydroxy, BYI08330-monohydroxy and BYI08330-enol glucoside in cotton gin trash, in apple fruit and in lettuce using aged radioactive residues, DACO: 7.2.1, 7.2.4
1314313	2005, Metabolism of (azaspirodecenyl-3-^{14}C)BYI08330 in apple after spray application, MEF-028/04 (and Study No. M1731298-1), MRID: 469044-80, DACO: 6.3
1314326	2006, Analytical method 00966 for the determination of residues of BYI 08330, BYI08330-enol, and BYI08330-enol-GA in/on matrices of animal origin by HPLC-MS/MS, MR-150/05 (Method No. 00966), MRID: 469044-92, DACO: 7.2.1,8.2.2.4

1314349	2006, Storage stability of BYI 08330 residues in plant matrices of rotational crops, MEF-06/155 (Study No. M9991559-7), MRID: 469044-97, DACO: 7.3
1314377	2006, Analytical method 00929 for the determination of residues of BYI08330-ketohydroxy-alcohol, BYI08330-desmethyl-ketohydroxy and BYI08330-desmethyl-di-hydroxy in/on plant material by HPLC-MS/MS, MR-026105 (Method No. 00929), MRID: 469044-94, DACO 7.2.1
1314401	2006, Analytical method 00969 for the determination of residues of BYI08330-enol in/on matrices of animal origin by HPLC-MS/MS, MR-160/05 (Method No. 00969), DACO: 7.2.1,7.2.4
1314443	2006, BYI08330 - request for waiver of the requirements for poultry feeding study and analytical method for the determination of BYI08330 residues in poultry meat and eggs, RAFNPO11, MRID: 469044-91, DACO: 7.5,7.6
1314445	2006, BYI08330 150 OD - Magnitude of the residue on potato processed commodities, RAFNY020, MRID: 469045-24, DACO: 7.4.5
1314446	2006, BYI08330 150 OD - Magnitude of the residue on apple processed commodities, RAFNY014, MRID: 469045-20, DACO: 7.4.5
1314447	2006, BYI08330 150 OD - Magnitude of the residue lactating cows, RAFNX014, MRID: 469045-01, DACO: 7.5,7.6
1314450	2006, Amended report - BYI08330 150 OD - Magnitude of the residue on citrus processed commodities, RAFNY016, MRID: 469045-22, DACO: 7.4.5
1314451	2006, BYI08330 150 OD and BYI08330 240 SC - Magnitude of the residue on potato, RAFNY028, MRID: 469045-19, DACO: 7.4.1,7.4.2,7.4.6
1314452	2006, BYI08330 100 OD - Magnitude of the residue on tomato processed commodities, RAFNY013, MRID: 469045-12, DACO: 7.4.5
1314485	2006, BYI08330 150 OD and BYI08330 240 SC - Magnitude of the residue on stone fruit (crop group 12 - including residue reduction samples), RAFNY001, MRID: 469045-13, DACO: 7.4.1,7.4.2,7.4.6
1314487	2006, BYI08330 150 OD and BYI08330 240 SC - Magnitude of the residue in/on leafy vegetables, RAFNY002, MRID: 469045-08, DACO: 7.4.1,7.4.2,7.4.6
1314488	2006, BYI08330 150 OD and BYI08330 240 SC - Magnitude of the residue in/on brassica leafy vegetables (crop subgroup 5A, head and stem brassica, and 5B, leafy brassica greens) including residue reduction information, RAFNY003, MRID: 469045-09, DACO: 7.4.1
1314489	2006, BYI08330 150 OD and BYI08330 240 SC - Magnitude of the residue in/on curcubit vegetables (crop group 9, including residue reduction information), RAFNY007, MRID: 469045-11, DACO: 7.4.1,7.4.2,7.4.6
1314490	2006, BYI08330 150 OD and BYI08330 240 SC - Magnitude of the residue on citrus (crop group 10, citrus fruits; includes residue reduction samples), RAFNY008, MRID: 469045-14, DACO: 7.4.1,7.4.2,7.4.6
1314492	2006, BYI08330 150 OD and BYI08330 240 SC - Magnitude of the residue on pome fruit (apple and pear), RAFNY009, MRID: 469045-15, DACO: 7.4.1,7.4.2,7.4.6
1314494	2006, BYI08330 150 OD and BYI08330 240 SC - Magnitude of the residue on hops, RAFNY022, MRID: 469045-18, DACO: 7.4.1,7.4.2,7.4.6
1314516	2006, BYI08330 150 OD and BYI08330 240 SC - Magnitude of the residue on

	fruiting vegetables (crop group 8 - tomato, bell pepper, non-bell pepper) (including residue reduction information), RAFNY006, MRID: 469045-10, DACO: 7.4.1,7.4.2,7.4.6
1314587	2006, BYI08330 150 OD - Magnitude of the residue on plum processed commodities, RAFNY018, MRID: 469045-23, DACO: 7.4.5
1314606	2006, FDA PAM Multiresidue method (MRM) testing for BYI08330 (Spirotetramat) and eight metabolites, RAFNP007, MRID: 469044-96, DACO: 7.2.1,7.2.4
1314608	2006, BYI08330 150 OD and BYI08330 240 SC - Magnitude of the residue in field rotational crops (limited), RAFNY019, MRID: 469045-26, DACO: 7.4.4
1314610	2006, BYI08330 150 OD - Magnitude of the residue in/on grapes processed commodities, RAFNY015, MRID: 469045-21, DACO: 7.4.5
1314614	2006, Indepedent method validation of Bayer Method No.00966 (Report No.MR-150/05) BYI08330: Analytical method 00966 for the determination of residues of BYI08330, BYI08330-enol, and BYI08330-enol-GA in/on matrices of animal origin by HPLC-MS/MS. DACO 7.2.1.
1314621	2006, BYI08330 150 OD and BYI08330 240 SC - Magnitude of the residue on tree nuts (crop group 14), RAFNY010, MRID: 469045-16, DACO: 7.4.1,7.4.2,7.4.6
1314622	2006, BYI08330 150 OD and BYI08330 240 SC - Magnitude of the residue in/on grapes, RAFNY011, MRID: 469045-17, DACO: 7.4.1,7.4.2,7.4.6
1314624	2006, Independent laboratory validation of the residue analytical method: "Analytical method 00857 for the determination of residues of BYI08330 (parent compound and total residue of BYI08330), BYI08330-enol, BYI08330-ketohydroxy, BYI08-mono-hydroxy and BYI 08330-enol-Glc metabolite in/on plant material by HPLC-MS/MS." MRID 46904489, DACO 7.2.1, 7.2.2, 7.2.3
1314662	2006, Storage stability of BYI 08330 and its metabolites BYI08330-enol, BYI08330- ketohydroxy, BYI08330-mono-hydroxy and BYI08330-enol-glucoside in/on orange (juice) and prunes (fruit) for 5 months, MR-06/076 (Study No. P642064705), MRID: 469044-97, DACO 7.3
1314682	2005, Analytical Method 00857/M003 for the determination of residues of BYI 08330 and BYI08330-ketohydroxy metabolite in/on plant material by HPLC-MS/MS, MR-098/05 (Method No. 00857/M003), DACO: 7.2.1,8.2.2.4
1314689	2005, Supplement E001 of the analytical method 00857 for the determination of residues of BY08330(parent compound and total residue of BYI08330), BYI08330-enol, BYI08330-ketohydroxy, BYI08330-mono-hydroxy and BYI08330-enol-Glc metabolite in/on plant material HPLC-MS/MS, MR-148/04, DACO: 7.2.1,8.2.2.4
1314696	2006, [Azaspirodecenyl-3-^{14}C] BYI 08330: Extraction efficiency testing (radiovalidation) of the residue method (00929) for the determination of BYI 08330-ketohydroxy-alcohol, BYI 08330-desmethyl-ketohydroxy and BYI 08330-desmethyl-di-hydroxy residues in plant samples using aged radioactive residues, MRID 46904506, DACO 7.2.1, 7.2.2, 7.2.3
1314701	2006, Metabolism of [azaspirodecenyl-3-^{14}C]BYI 08330 in confined rotational crops, MEF-05/288 (and Study No. M1301259-1), MRID: 469045-02, DACO: 6.3

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1314453	2006, Determination of Dislodgeable Foliar Residue on Grapes and Hops Treated with BYI08330 150 OD, M-277037-01-1, DACO 5.9
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3.0 Impact on the Environment

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1314255	2005, BYI08330[azaspirodecenyl-3-14C]: Anaerobic aquatic metabolism, M-261943-01-1, MRID: 469044-11, DACO: 8.2.3.5.6
1314287	2005, Aerobic degradation/metabolism of BYI8330 in four different soils (Amendment No. 1), MEF-04/169 (Study No. M1251207-8), MRID: 469044-08, DACO: 8.2.3.4.2
1314304	2006, Outdoor metabolism of [azaspirodecenyl-3-14C]BYI08330 in two soils, MEF-06/041 (Study No. M1251374-3), MRID: 469044-09, DACO: 8.2.3.4.2
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1314317	2005, Adsorption/desorption of BYI08330-cis-enol in five different soils (final report), IM2000 (Study No. BAY55), MRID: 469044-29, DACO: 8.2.4.2
1314324	2006, [Azaspirodecenyl-3-14C]- and [azaspirodecenyl-5-14C]-labeled BYI08330-cis-enol: Comparative aerobic soil metabolism/degradation in four soils, MEF-05/157 (Study No. M1251359-6), MRID: 469044-28, DACO: 8.2.3.4.2
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4.0 Value

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