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Evaluation Report

Spiromesifen

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Overview

Proposed Registration Decision for Spiromesifen

Health Canada's Pest Management Regulatory Agency (PMRA), under the authority of the *Pest Control Products Act*[1] and Regulations, has granted conditional registration for the sale and use of Spiromesifen Technical Insecticide/Miticide and Forbid 240 SC Insecticide/Miticide containing the technical grade active ingredient spiromesifen to control mites and whiteflies on greenhouse and outdoor ornamentals, on greenhouse and field vegetables as well as on strawberries.

Current scientific data from the registrant, scientific reports and information from other regulatory agencies were evaluated to determine if, under the proposed conditions of use, the product has value and does not present an unacceptable risk to human health or the environment.

This report summarizes the information evaluated and provides the results of the evaluation as well as the reasons for the conditional registration decision, with an outline of the additional scientific information required from the applicant. It also describes the conditions of registration that applicants must meet to ensure that the health and environmental risks as well as the value of these pest control products are acceptable for their intended use.

This overview describes the key points of the evaluation, while the Science Evaluation section provides detailed technical information on human health, environmental and value assessment of spiromesifen as well as Forbid 240 SC Insecticide/Miticide .

What Does Health Canada Consider When Making a Registration Decision?

The key objective of the *Pest Control Products Act* is to prevent unacceptable risks[2] to people and the environment from the use of pest control products. Health or environmental risk is considered acceptable 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 conditions or proposed conditions of registration. The Act also requires that products have value[3] when used according to the label directions. Conditions of registration may include special precautionary measures on the product label to further reduce risk.

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1 As per subsection 28(1) of the *Pest Control Products Act*.

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

3 "Value" as defined by subsection 2(1) of the *Pest Control Products Act* (http://laws.justice.gc.ca/en/P-9.01/92455.html): "...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".

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 www.pmra-arla.gc.ca.

What Is Spiromesifen?

Spiromesifen is an insecticide applied directly onto leaves to control mites and whiteflies. It is applied to greenhouse and outdoor ornamentals, greenhouse and field vegetables as well as strawberries using ground and, in some instances, aerial application equipment. Spiromesifen inhibits lipid biosynthesis in target insects and is effective against all immature life stages. It may have indirect effects on adults of some target insect species.

Health Considerations

Can Approved Uses of Spiromesifen Affect Human Health?

Spiromesifen is unlikely to affect your health when used according to the label directions.

People could be exposed to spiromesifen through diet (food and water) or when handling and applying Forbid 240 SC Insecticide/Miticide. When assessing health risks, the PMRA considers two key factors: the levels at which no health effects occur 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).

Toxicology studies in laboratory animals describe potential health effects from varying levels of exposure to a chemical and identify the dose at which 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 products containing spiromesifen are used according to the label directions.

The technical grade active ingredient spiromesifen caused allergic skin reactions in animals. Consequently, the statement "Potential Dermal Sensitizer" is required on the label for the technical grade active ingredient. The end-use product Forbid 240 SC Insecticide/Miticide caused slight toxicity in animals when inhaled. Consequently, the statement "Caution—Poison" is required on the label for the end-use product. Spiromesifen did not cause cancer in animals and was not genotoxic[4]. Health effects in

[4] Genotoxic chemicals are those capable of causing damage to DNA. Such damage can potentially lead to the formation of a malignant tumour, but DNA damage does not lead inevitably to the creation of cancerous cells.

animals given daily doses of spiromesifen over long periods of time included effects on the spleen, liver, uterus, thyroid gland and adrenal gland. When spiromesifen 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 spiromesifen than the adult animal. Effects on the young animal, however, were slightly more severe than those observed in parental animals after the parental animals were given daily doses of spiromesifen before mating, during pregnancy and while providing nourishment to the young animal through lactation. Signs of potential neurotoxicity were observed at doses that caused other effects in test animals. 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. Only those uses where exposure is well below levels that cause no effects in animal testing are considered acceptable for registration.

Residues in Water and Food

Dietary risks from food and water are not of concern.

Reference doses define levels to which an individual can be exposed over a single day (acute) or lifetime (chronic) and expect no adverse health effects. Generally, dietary exposure from food and water is acceptable if it is less than 100% of the acute reference dose or chronic reference dose (acceptable daily intake). An acceptable daily intake is an estimate of the level of daily exposure to a pesticide residue that, over a lifetime, is believed to have no significant harmful effects.

Aggregate dietary intake estimates (food plus water) revealed that the general population and infants, the subpopulation which would ingest the most spiromesifen relative to body weight, are expected to be exposed to less than 84% of the acceptable daily intake. Based on these estimates, the chronic dietary risk from spiromesifen is not of concern for all population subgroups. The results of the cancer studies were negative; therefore, a chronic cancer dietary risk assessment was not required.

Animal studies revealed no acute health effects. No endpoint of concern attributable to a single dose was identified. Consequently, a single dose of spiromesifen is not likely to cause acute health effects in the general population (including infants and children).

The *Food and Drugs Act* prohibits the sale of food containing a pesticide residue that exceeds the established maximum residue limit (MRL). Each MRL value determines the maximum concentration in parts per million (ppm) of a pesticide allowed in or on certain foods. Pesticide MRLs are established for *Food and Drugs Act* purposes 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.

No residue trials were conducted in Canada. However, a significant number of residue trials conducted throughout the United States and Europe using spiromesifen on field

corn, strawberry, leafy green vegetables, tuberous and corm vegetables, brassica leafy vegetables, cucurbit vegetables, fruiting vegetables, greenhouse cucumber, greenhouse tomato and greenhouse pepper was acceptable. The MRLs for spiromesifen can be found in the Science Evaluation section of this Evaluation Report.

Workplace Risks From Handling Forbid 240 SC Insecticide/Miticide

Occupational risks are not of concern when Forbid 240 SC Insecticide/Miticide is used according to the label directions, which include protective measures.

Farmers and pesticide applicators mixing, loading or applying Forbid 240 SC Insecticide/Miticide as well as workers entering fields or greenhouses of freshly treated crops can come in direct contact with spiromesifen on the skin or through inhalation of spray mists. Therefore, the label specifies that anyone mixing or loading Forbid 240 SC Insecticide/Miticide must wear a long-sleeved shirt, pants, chemical-resistant gloves, a respirator with appropriate filter and goggles or a face shield and that anyone applying the product must wear a long-sleeved shirt and pants. Based on these label statements, risk to farmers, applicators or workers is not a concern.

For members of the general population that are at pick-your-own facilities, exposure is not of concern because there were no acute concerns for spiromesifen identified in the toxicological database.

Environmental Considerations

What Happens When Spiromesifen Is Introduced Into the Environment?

Spiromesifen is toxic to terrestrial plants and aquatic organisms. Therefore, buffer zones are required during application.

Spiromesifen enters the environment when used as an insecticide on a variety of crops including field corn, cucurbit vegetables, fruiting vegetables, brassica leafy vegetables, leafy green vegetables, tuberous and corm vegetables and strawberries. Spiromesifen is not persistent to slightly persistent in soil (depending on soil characteristics) and slightly persistent in water, while the major transformation product, BSN 2060-enol, is persistent in water and slightly to moderately persistent in soil (depending on soil characteristics). Spiromesifen is not expected to leach through the soil profile beyond 30 cm; therefore, it is not expected to enter groundwater. In contrast, BSN 2060-enol is mobile and expected to leach into and enter groundwater. Based on its low volatility, spiromesifen residues are not expected in the air.

Spiromesifen does not present a risk to wild mammals, birds, marine invertebrates, algae or aquatic plants. However, spiromesifen does affect terrestrial plants, predators and parasites, daphnia, freshwater and marine fish as well as amphibians in adjacent areas. Therefore, to protect from the effects of spray drift, ground buffer zones of 2 to 10 metres (depending on crop and spray technology) for freshwater habitats, 1 metre for marine

habitats and 1 to 2 metres for terrestrial habitats; and aerial buffer zones of 25 to 350 metres for freshwater habitats, 1 to 10 metres for marine habitats and 35 to 40 metres for terrestrial habitats are required to protect sensitive aquatic species and non-target plant species in adjacent habitats.

Value Considerations

What Is the Value of Spiromesifen?

Spiromesifen, an insecticide/miticide, controls specific mites and whiteflies on greenhouse vegetables and ornamentals, field corn, cucurbits, leafy green vegetables, leafy brassica vegetables, tuberous and corm vegetables and strawberries.

Spiromesifen controls specific mites and whiteflies on a variety of crops, in both greenhouses and outdoors. It is also compatible with current management practices and conventional crop production systems. Growers are familiar with the monitoring techniques to determine if and when applications are needed

There are no insecticides or miticides from the same class as spiromesifen currently registered for use on the listed crops. Therefore, spiromesifen offers a new class for resistance management purposes. When applied according to the label directions, spiromesifen controls effectively the following pests: two-spotted spider mite, banks grass mite, broad mite and whiteflies (including silverleaf, sweet potato and greenhouse).

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.

Key Risk-Reduction Measures

Human Health

- As there is a concern with users coming into direct contact with spiromesifen on the skin or through inhalation of spray mists, anyone mixing or loading Forbid 240 SC Insecticide/Miticide must wear a long-sleeved shirt, pants, chemical-resistant gloves, a respirator with appropriate filter and goggles or a face shield. Anyone applying the product must wear a long-sleeved shirt and pants.

Environment

- Forbid 240 SC Insecticide/Miticide cannot be sprayed within 1 to 40 metres of susceptible non-target plant species and between 1 to 350 metres of susceptible aquatic organisms. The distance allowed depends on the type of spray equipment used to apply the product, the type of habitat and the crop being sprayed with the product.

What Additional Scientific Information Is Required?

Although the risks and value have been found acceptable when all risk-reduction measures are followed, the applicant must submit additional scientific information as a condition of registration. More details are presented in the Science Evaluation section of this Evaluation Report or in the Section 12 Notice associated with these conditional registrations. The applicant must submit the following information within the time frames indicated.

Human Health

- Storage stability data for the commodities analyzed in the Field Accumulation in Rotational Crops studies to validate the 22-month storage intervals. The study must be submitted to the PMRA upon its completion, no later than June 2008.

Other Information

As these conditional registrations relate to a decision on which the public must be consulted[5], the PMRA will publish a consultation document when there is a proposed decision on the applications to convert the conditional registrations to full registrations or on the applications to renew the conditional registrations, whichever occurs first.

The test data cited in this Evaluation Report (i.e. the test data relevant in supporting the registration decision) will be made available for public inspection when the decision is made to convert the conditional registrations to full registrations or to renew the conditional registrations (following public consultation). If more information is required, please contact the PMRA's Pest Management Information Service by phone (1-800-267-6315) or by e-mail (pmra_infoserv@hc-sc.gc.ca).

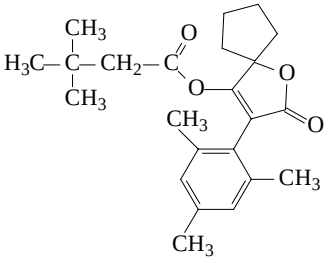
[5] As per subsection 28(1) of the *Pest Control Products Act*.

Science Evaluation

Spiromesifen

1.0 The Technical Grade Active Ingredient, its Properties and Uses

1.1 Identity of the Technical Grade Active Ingredient

Active substance		Spiromesifen
Function		Insecticide/Miticide
Chemical name		
1.	**International Union of Pure and Applied Chemistry (IUPAC)**	3-mesityl-2-oxo-1-oxaspiro[4.4]non-3-en-4-yl 3,3-dimethylbutyrate
2.	**Chemical Abstracts Service (CAS)**	2-oxo-3-(2,4,6-trimethylphenyl)-1-oxaspiro[4.4]non-3-en-4-yl 3,3-dimethylbutanoate
CAS number		283594-90-1
Molecular formula		$C_{23}H_{30}O_4$
Molecular weight		370.48
Structural formula		
Purity of the active ingredient		98.4% nominal (limits: 96.5% - 100.0%)

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

Technical Product—Spiromesifen Technical Insecticide/Miticide

Property	Result
Colour and physical state	Colourless solid
Odour	Intensive, characteristic odour

Property	Result	
Melting point	96.7°C	
Boiling point or range	Not applicable	
Density	1.13 g/mL	
Vapour pressure	7×10^{-6} Pa at 20°C 1×10^{-5} Pa at 25°C	
Henry's law constant at 20°C	1.9×10^{-7} atm·m^3/mol	
Ultraviolet (UV)—visible spectrum	λ_{max} = 214 nm	
Solubility in water at 20°C	0.13 mg/L	
Solubility in organic solvents at 20°C (g/L)	**Solvent** n-Heptane Xylene Dichloromethane 2-Propanol 1-Octanol Polyethylene glycol Acetone Ethyl acetate Acetonitrile Dimethylsulfoxide	**Solubility** 23 > 250 > 250 110 60 22 > 250 > 250 > 250 55
n-Octanol–water partition coefficient (K_{ow})	log K_{ow} = 4.55 K_{ow} = 36000	
Dissociation constant (pK_a)	No acidic or basic properties in water between pH 4 and 9.	
Stability (temperature, metal)	The TGAI is thermally stable at ambient temperature under air. No exothermic reaction occurred until 300°C. A weight loss was observed starting at 150°C. The TGAI is stable in presence of aluminum, copper, brass, plain steel, stainless steel and tin.	

End-Use Product—Forbid 240 SC Insecticide/Miticide

Property	Result
Colour	Light tan
Odour	Musty, earthy odour with a bleach like accent

Property	Result
Physical state	Liquid
Formulation type	Suspension
Guarantee	240 g/L (limits: 233 g/L–247 g/L)
Container material and description	High density polyethylene containers, 500 mL and 5 L
Density	1.029 g/cm^3 at 20°C
pH of 10% dispersion in water	4.6
Oxidizing or reducing action	The product does not contain any oxidizing or reducing agents.
Storage stability	The product is stable when stored for one year at ambient warehouse conditions in commercial packaging.
Explodability	The product is not expected to be explosive.

1.3 Directions for Use

Forbid 240 SC Insecticide/Miticide is intended for use in the greenhouse on ornamentals, tomato, cucumber and pepper and for use in the field on corn, strawberries, tuberous and corm vegetables (crop group 1C), cucurbits (crop group 9), leafy green vegetables (crop group 4A) and brassica leafy vegetables (crop group 5) to control mites and whiteflies. The product is applied as a foliar treatment via ground application equipment, but may also be applied by plane (fixed wing or rotary) to outdoor field crops (except ornamentals). The application rate and maximum number of applications varies depending on the crop (Table 1.3.1).

Table 1.3.1 Insect Control Claims for Spiromesifen

Crop	Pest	Rate	Maximum Number of Applications per Season
Greenhouse vegetables (tomatoes, pepper and cucumber)	Two-spotted spider mite	0.03–0.05% (0.072–0.120 g a.i./L)	2 times per crop cycle
	Whiteflies	0.03–0.05% (0.072–0.120 g a.i./L)	

Crop	Pest	Rate	Maximum Number of Applications per Season
Greenhouse ornamentals	Two-spotted spider mite	0.03% (0.072 g a.i./L)	2 times per crop cycle
	Whiteflies	0.03% (0.072 g a.i./L)	
Outdoor ornamentals	Mites	0.03% (0.072 g a.i./L)	3
	Whiteflies	0.03% (0.072 g a.i./L)	
Field Corn	Two-spotted spider mite Banks grass mite	96–144 g a.i./ha	2
Cucurbit Vegetables (Crop Group 9)	Two-spotted spider mite	120–144 g a.i./ha	3
	Whiteflies	120–144 g a.i./ha	
Fruiting Vegetables (Crop Group 8)	Two-spotted spider mite Broad mite	120–144 g a.i./ha	3
	Whiteflies	120–144 g a.i./ha	
Leafy Greens Vegetables (Crop Subgroup 4A)	Whiteflies	120–144 g a.i./ha	3
Brassica Leafy Vegetables (Crop Group 5)	Whiteflies	120–144 g a.i./ha	3
Tuberous and corm vegetables (Crop subgroup 1C)	Two-spotted spider mite	120–144 g a.i./ha	2
	Whiteflies	120–144 g a.i./ha	
Strawberry	Two-spotted spider mite	211–278 g a.i./ha	3
	Whiteflies	211–278 g a.i./ha	

1.4 Mode of Action

Spiromesifen is classified as a Group 23 Insecticide (Insecticide Resistance Action Committee, 2005) and has a similar mode of action as the currently registered active ingredient, spirodiclofen (resistance management group 23), which functions by inhibiting lipogenesis. Spiromesifen is most active against immature life stages, including eggs and has both ingestion and contact activity, depending on the target insect. It may have indirect effects on adults of some target insect species. Due to its high lipophilicity, spiromesifen has contact efficacy against spider mites, but has both contact and feeding activity against whiteflies.

2.0 Methods of Analysis

2.1 Methods for Analysis of the Technical Grade of Active Ingredient

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

2.2 Method for Formulation Analysis

The method provided for the analysis of the active ingredient in the formulation has been validated and assessed to be acceptable for use as an enforcement analytical method.

2.3 Methods for Residue Analysis

A high-performance liquid chromatography method with dual mass spectrometry (HPLC-MS/MS) was developed and proposed for data generation in plant (primary crop) matrices, with a modification of the same method proposed for enforcement purposes. The enforcement method is the same method as the data-gathering method with minor modifications that were incorporated during the independent laboratory validation (ILV). The basic principal of the method was unchanged. Other HPLC-MS/MS methods were developed and proposed for both data gathering and enforcement purposes; one for animal matrices and one for rotational crop matrices. All these methods fulfilled the requirements with regards to specificity, accuracy and precision at the respective method limit of quantitation. Acceptable recoveries (70–120%) were obtained in primary crop, rotational crop and animal matrices, environmental media and body fluids. Adequate extraction efficiencies were demonstrated using radiolabelled lettuce and tomato samples analysed with the primary crop data-gathering method, turnip roots and wheat straw samples analysed with the rotational crop enforcement method and goat milk, goat liver and goat fat samples analysed with the animal enforcement method. Spiromesifen, BSN 2060-enol and BSN 2060-4-hydroxymethyl were analysed according to the Food and Drug Administration's (FDA) Multiresidue Method Testing guidelines in Pesticide Analytical Methods (PAM) Volume I, Appendix II (January 1994). The multiresidue methods tested (Protocols D, E and F) may be suitable for analysis of spiromesifen in non-oily and fatty commodities. These methods are not suitable for BSN 2060-enol or BSN 2060-4-hydroxymethyl. (Appendix I, Table 1)

3.0 Impact on Human and Animal Health

3.1 Toxicology Summary

The PMRA conducted a detailed review of the toxicological database for spiromesifen. The database is complete, consisting of the full array of laboratory animal (in vivo) and cell culture (in vitro) toxicity studies currently required for health 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 characterize the toxicity of this pest control product.

Spiromesifen Technical Insecticide/Miticide is of low acute toxicity by the oral, dermal and inhalation routes in Wistar rats. It was non-irritating when applied to the skin and eyes of Himalayan rabbits. Spiromesifen was positive for dermal sensitization in guinea pigs using the maximization method.

Forbid 240 SC Insecticide/Miticide formulation is of low acute toxicity by the oral and dermal routes and of slight toxicity by the inhalation route in Wistar rats. It was non-irritating when applied to the skin and eyes of Himalayan rabbits. Results of skin sensitization testing in guinea pigs using the Buehler method were negative.

The pharmacokinetic behaviour of spiromesifen was characterized by a rapid absorption and elimination from the plasma in rats. Approximately 50% of the orally administered dose was absorbed. Following administration of single and repeated low doses, approximately 40% of the administered dose was excreted in the urine, 55 to 57% was excreted in the feces and 7% was excreted with the bile. Excretion in the feces was much greater (approximately 90%) following administration of a single high dose. Approximately 90% of the administered dose was eliminated within the first 24 hours.

Spiromesifen was extensively metabolized by the rat. Spiromesifen was initially metabolized to the keto-enol by loss of the dimethylbutyric acid moiety. Both the phenyl and the cyclopentyl rings were hydroxylated and the methyl groups on the phenyl ring were ultimately oxidized to a carboxylic acid. No conjugation with either glucuronic acid or sulfate was observed and there was no evidence of cleavage between the phenyl and hydrofuranone rings. The analysis of metabolites in urine, feces and bile revealed the same metabolites in all test groups. Sex-related differences between the test groups were found in the quantitative distribution of the same metabolites in the excreta. The main metabolite in the excreta of female rats of the low dose groups was the BSN 2060-enol, whereas the main metabolite in the excreta of male rats of the low dose groups was the BSN 2060-4-hydroxymethyl. These metabolites were largely recovered in the bile and urine. The predominant moiety recovered in feces was the unmetabolized test material.

Additional pharmacokinetic measurements were conducted in the repeat dose dietary studies in the dog. Plasma kinetics revealed that spiromesifen was rapidly metabolized to BSN 2060-enol with no detection of the parent compound. The plasma levels for this metabolite remained stable over a 24-hour period after feeding, increased with dose and with duration of dosing, but at the end of the 1-year study were lower than at week 12, indicating the absence of any relevant cumulative potential of this metabolite in dogs.

Spiromesifen inhibits acetyl CoA carboxylase, an enzyme that catalyzes the carboxylation of acetyl CoA to malonyl CoA, which is one of the first steps of fatty acid biosynthesis. As a consequence of the biological mode of action, decreased plasma cholesterol levels were seen in short-term and long-term studies in rodents. This was one of the most sensitive parameters affected, particularly in mice. In the mouse and also at higher doses in the rat, effects indicative of depleted reservoirs of cholesterol in the adrenal gland were noted and included cytoplasmic eosinophilia in zona fasciculata cells, decreased adrenocortical ceroid deposits and decreased normal diffuse fatty changes. In the rat, females appeared to be more sensitive to alterations in

cholesterol and triglyceride levels than male rats. Rats also exhibited decreased plasma triglyceride levels and decreased hepatic periportal fat storage.

The thyroid gland, liver and adrenal gland were identified as the primary target organs in dietary studies conducted with the rat, mouse and/or dog. The rat appeared to be most sensitive to effects on the thyroid gland and spleen, while the mouse often displayed effects on the adrenal gland at lower doses than the rat. The liver was the primary target organ in the dog.

In addition to hepatic enzyme (including UDP-glucuronyl transferase) induction and the effects noted above related to altered cholesterol synthesis, several adverse effects on the liver were also observed in the rat, mouse and dog at higher doses. These effects included altered weight, cytoplasmic changes, hypertrophy and necrosis.

In the rat, effects on the thyroid gland included decreased levels of T4 and T3, increased levels of TSH, increased thyroxin binding capacity (TBC), follicular cell hypertrophy, colloidal alterations and ectasia. Dogs also exhibited reduced T4 and elevated T3 that were not accompanied by histological changes.

Additional effects noted in the adrenal gland of mice following subchronic dietary exposure included weight changes, reduced fine vesiculation, discolouration and hypertrophy of zona fasciculata cells. Following chronic dietary exposure, mice displayed reduced subcapsular hyperplasia (Type A) and enlargement of the adrenal gland. Rats also exhibited cytoplasmic changes in the zona fasciculata cells after short-term exposure at very high doses. Adrenal effects in the dog were limited to cortical vacuolation.

Several hematological parameters were affected in rodents after short-term dietary exposure to spiromesifen. Effects included decreased values for haemoglobin, mean corpuscular volume, mean corpuscular haemoglobin and hematocrit as well as reduced thrombocyte counts, elongated clotting time and changes in differential leukocyte counts. Additional effects at very high doses indicating disturbance of the hematopoietic system included decreased siderin storage in the red pulp of the spleen, increased hematopoiesis in the spleen and increased number of fat cells in bone marrow. In the subchronic rat study, the effects on the bone marrow and spleen were found to be reversible, while some haematological parameters continued to be affected after cessation of dosing.

Effects on the small intestine and kidney were only observed in rat short-term studies at high to very high doses. Changes in the small intestine included white mucus/white mucosa coverings in the duodenum and/or jejunum and cytoplasmic vacuolization (lipid droplets) in the enterocytes of duodenal and jejunal mucosa. In the kidney, weight changes, increased hyaline droplets in the proximal tubules and mineralization of Henle’s loops were noted. All of these effects were reversible during the recovery period in the subchronic study.

Effects on the immune system were seen at high doses in rat short-term studies. The observed changes included effects on the thymus (weight change, atrophy, reduced medullary area, reduced lymphocyte counts, indistinct corticomedullary junction), spleen (weight changes, lymphoid atrophy, hypocellularity in the periarteriolar lymphocyte sheaths, decreased spleen cell

counts) and on several morphological immunological parameters (reduced cell markers for T helper and T cells, increased expression of cell markers for B cells and macrophages, reduced antibody titers, increased macropahge activation in splenic cells). All observed changes were assessed as secondary to the marked general systemic toxicity. As spleen effects were seen in several toxicity studies, the registrant pursued specialized immunotoxicity studies in the rat and mouse that showed no effects on plaque forming assays. However, these studies were considered supplemental due to the lack of organ weight measurements. Although the results from the toxicology data are indicative of potential immunotoxicity, the doses selected for risk assessment are protective of immunotoxic effects.

The uterus was detected as another target, but only in the rat long-term studies at the highest dietary exposure level. Effects on the uterus included increased weight and girth, vaginal bleeding, dilation, increased incidence of uterine nodules and endometrial hyperplasia of the cervix, as well as increased severity of focal glandular hyperplasia, endometrial stromal hyperplasia and hypertrophic luminal epithelium.

No primary reproductive effects following exposure to spiromesifen was determined in multigeneration studies in rats and in developmental toxicity studies in rats and rabbits. In a two-generation reproductive toxicity study, offspring effects were observed at the same doses that produced maternal toxicity. In the rat and rabbit developmental toxicity studies, no developmental effects were seen in the absence of maternal toxicity.

In a first two-generation study in rats, parental toxicity (decreased body weight, decreased vacuolation in the zona glomerulosa of the adrenal gland, follicular cell hypertrophy and colloidal alteration in the thyroid gland and decreased periportal fat content in the liver) and neonatal toxicity (decreased body, spleen and thymus weights) were only observed at the highest dietary exposure level. Lower lactation indices were observed in all dose groups in the second generation but did not occur in a dose-dependent manner. As similar results had been seen in a concurrent multi-generation study with a different substance at the same laboratory, it was concluded that this effect was not related to the spiromesifen exposure but was apparently a problem with the source of rat used. Therefore the study was repeated using a different source of rats.

The second study revealed acceptable lactation indices and similar effects in parents and offspring as those noted in the first study, except that effects were noted at a lower dose in the repeat study than in the original study. Parental toxicity was indicated by reduced body and spleen weights at the LOAEL, while thyroid gland (follicular cell hypertrophy, colloidal alteration), liver (increased weight, periportal basophilia, hepatocellular hypertrophy) and adrenal gland (atrophy of the zona glomerulosa region) effects were noted at the highest dose tested. Neonatal toxicity (decreased body, spleen and thymus weights) were observed at the LOAEL as well. Reproductive toxicity (increased number of ovarian primordial follicles, decreased number of ovarian growing follicles and delayed sexual maturation of weanlings) was only observed secondarily to general systemic toxicity at the highest dose. Both two-generation studies showed that these effects had no impact on the reproductive performance of the rats. However, indications of qualitative sensitivity of the young were provided by the results of the

repeat study, in which body and organ weight decrements were noted in F_1 offspring at a dose which caused only slight reductions in the spleen weight of females in the parental generation.

In the developmental toxicity studies in rats and rabbits, a “more progressed” ossification of several bones, including some bones of the skull in rats, was noted at doses that results in body weight decrements and reduced feed intake in maternal animals. At higher doses in the rat, maternal animals exhibited convulsions while a decreased percentage of male fetuses was observed developmentally. In rabbits, higher doses resulted in abortions and total litter resorptions as well as clinical signs of toxicity in maternal animals.

No adverse systemic effects or local skin reactions were seen in a dermal study with rats exposed to 1000 mg/kg bw/day over a 4-week period. In a 5-day inhalation toxicity study with rats, mortality in females, clinical signs of toxicity, abnormal reflexes, impaired blood clotting ability and effects on the respiratory system (increased relative lung weight, appearance of lungs being less collapsed, dark red foci in the lung, white viscous content in the trachea and nasal cavity) as well as on the liver (increased serum liver enzymes, pale) and spleen (pale, decreased weight) were noted at the highest dose tested (134 mg/kg bw/day). No adverse effects were noted in a 28-day inhalation toxicity study in rats up to 21.1 mg/kg bw/day. It should be noted that adverse effects following inhalation exposure to spiromesifen occurred only at those doses where the relative humidity of the exposure chamber was approaching 30%; all other exposures occurred at relatively low humidity levels below the guideline minimum of 30%.

Effects indicative of potential neurotoxicity were observed at high doses in the 5-day inhalation study and in repeat dose dietary studies in the rat (28-day and 90-day studies) and were usually more prevalent and/or more severe in female rats than in male rats. These effects included reduced motility, spastic gait, increased reactivity, tremors, clonic-tonic convulsions, reduced activity, uncoordinated gait, laboured breathing, vocalization, avoidance reaction, piloerection, limp, cyanosis, squatted posture, aggressiveness and salivation. These effects appeared to be secondary to severe systemic toxicity and were not correlated with neuropathology. No evidence of neurotoxicity was indicated in the acute neurotoxicity study. In the subchronic neurotoxicity study, decreased landing foot splay was noted at a high dose along with clinical signs of neurotoxicity that were limited to one female. These findings do not indicate that spiromesifen is an overt neurotoxicant.

Spiromesifen was not oncogenic in rats and mice as a result of chronic dietary exposure and results were negative in a battery of mutagenicity assays. The incidence of uterine stromal polyps was slightly increased in female mice after 18 months of exposure to high dietary levels of spiromesifen. Given that spiromesifen is not considered to be genotoxic, that these tumours were benign and that there was no indication of treatment-related malignant uterine tumours or other treatment-related proliferative changes in the female reproductive tract of mice in this study, a margin approach will be used to ensure that adequate protection against this finding is provided by the risk assessment.

Effects indicative of endocrine system toxicity included the above-noted effects on the thyroid, uterus, adrenal gland and ovarian follicle counts. Female rats appeared to be more sensitive to the effects of spiromesifen as manifest through more severe and frequently occurring clinical

signs of toxicity as well as incidences of mortality noted at high doses. The toxicology database for spiromesifen did not include any assessment of thyroid toxicity in the young following in utero or early life exposure. As a result, there is residual uncertainty with respect to the thyroid response to spiromesifen exposure in the young. In order to protect for this uncertainty, a 3-fold factor was retained in the risk assessment. (Appendix I, Table 3)

3.2 Determination of Acceptable Daily Intake

The recommended acceptable daily intake (ADI) for spiromesifen is 0.007 mg/kg bw/day, calculated using the NOAEL of 2.2 mg/kg bw/day for males from the P generation of the two-generation reproductive toxicity study in the rat. Treatment-related effects noted at the LOAEL (8.8/14.2 mg/kg bw/day in males/females from the P generation) included decreased spleen weights in P adult females, decreased body weights in offspring of both generations during the lactation period, decreased spleen and thymus weights in male offspring of the F_1 generation, decreased body weight in F_1 adults of both sexes and decreased spleen weight in adult males of the F_1 generation. In this study, qualitative evidence of increased susceptibility of the young was observed as demonstrated by reduced body and organ weights in F_1 offspring at a dose that resulted in a less severe effect (slight decrease in spleen weight) in females that bore these offspring.

This study is considered appropriate for the determination of the ADI because it provides the lowest NOAEL in the database and it assesses the effects of exposure to spiromesifen on reproductive ability and on the developing young. This study is also of the appropriate duration and route of exposure.

The standard uncertainty factor (UF) of 100 is applied to account for interspecies extrapolation and any intraspecies variablity in toxicological responses when exposed to a chemical substance. Under the new *Pest Control Products Act* (PCPA), a threefold factor has been retained as a result of residual uncertainty in the toxicological database with regards to thyroid response in the young. This residual uncertainty could be addressed through the conduct of a study that examines thyroid toxicity in both adults and the young following in utero exposure.

The lowest dose that provides protection against effects on the endocrine system is the NOAEL of 3.3/3.8 mg/kg bw/day in males/females in the 18-month oncogenicity study in the mouse, in which adrenal gland effects (enlargement, eosinophilia of the zona fasciculata cells, decreased ceroid deposits in the adrenal cortex, decreased subcapsular hyperplasia and decreased incidence of diffuse fatty change) were noted at the LOAEL of 22/30 mg/kg bw/day in males/females. This ADI provides a margin of safety of 471 to the NOAEL in the 18-month oncogenicity study and is considered to be protective of potential endocrine toxicity. This ADI also provides adequate margins of safety to cover off any other endpoints of concern that were observed in the spiromesifen toxicological database, including developmental toxicity. (Appendix I, Table 4)

The ADI is calculated according to the following formula:

$$\text{ADI} = \frac{\text{NOAEL}}{\text{UF}} = \frac{2.2 \text{ mg/kg bw/day}}{300} = 0.007 \text{ mg/kg bw/day of spiromesifen}$$

3.3 Determination of Acute Reference Dose

An acute reference dose (ARfD) was not determined because an endpoint of concern attributable to a single exposure was not identified in the oral toxicity studies.

3.4 Occupational and Bystander Risk Assessment

3.4.1 Toxicological Endpoints and Dermal Absorption

3.4.1.1 Toxicological Endpoints

Occupational exposure to Spiromesifen is characterized as short-term to long-term in duration and may occur by the dermal and inhalation routes. Repeat dose dermal and inhalation toxicity studies did not account for the treatment-related reproductive endpoints noted in rats in the two-generation reproductive toxicity study. Therefore, the two-generation reproductive toxicity study in the rat with a NOAEL of 2.2 mg/kg bw/day was used for short-term to long-term inhalation and dermal exposure scenarios. A margin of exposure (MOE) of 300 is recommended based on a 100-fold uncertainty factor to account for interspecies extrapolation and intraspecies variability and an additional factor of 3-fold to protect for residual uncertainty with regard to thyroid response in the young. This endpoint and target MOE provide adequate protection to the mortality noted in the five-day inhalation toxicity study at 134 mg/kg bw/day; a margin of 3000 is provided to the next lowest dose of 20.7 mg/kg bw/day.

In addition, acute oral or dermal exposure of bystanders may occur in pick-your-own strawberry patches. No risk assessment for this exposure scenario was required as no endpoints of concern were identified following acute oral or dermal exposure to Spiromesifen.

Results of the acute and chronic tests conducted on laboratory animals with Spiromesifen and its associated end-use product Forbid 240 Miticide/Insecticide, as well as the toxicological endpoints selected for the human health risk assessment, are summarized in Tables 2, 3 and 4 of Appendix I.

3.4.1.2 Dermal Absorption

Dermal administration of Spiromesifen SC 480, containing ^{14}C spiromesifen, to five male rhesus monkeys resulted in a mean recovery of 2.15% of the dose in excreta (1.49 % in urine, 0.28 % in feces, 0.11 % in cage debris/rinse samples and 0.27 % in the pan wash/wipe and chair wipe) through 120 hours. The majority of the administered dermal dose was recovered from the application site (mean = 90.8 %) with 0.12% of the applied dose recovered in the tape strips.

In an exploratory study, dermal administration of Spiromesifen SC 480, containing ^{14}C spiromesifen, to a male rhesus monkey resulted in a dermally absorbed dose of 3.31% (1.72% in urine, 0.07% in feces,1.35% in cage debris/rinse samples and 0.17% in the cage wash/wipe) through 192 hours (US EPA DER, Feb. 17, 2004). However, 9.39% of the applied dose was recovered from the non-occlusive cover and therefore was not available for absorption. The majority of the administered dermal dose was recovered from the application site (94.9%) with

0.11% of the applied dose recovered in the tape strips. The overall recovery of radioactivity from the dermally dosed animal was 107.71%. The overall recovery of radioactivity for the intravenously dosed animal was 94.08%, indicating that 5.92% may have remained in the body.

Based on the average dose of test material found in the excreta in the five dermally dosed monkeys (2.15%) and the amount in the excreta for the dermally dosed animal in the pilot study (3.31%), a dermal absorption value of 3% is considered appropriate for use in a risk assessment.

3.4.2 Occupational Exposure and Risk

3.4.2.1 Mixer/Loader/Applicator Exposure and Risk

Exposure to workers mixing, loading and applying Forbid 240 SC Insecticide/Miticide to field crops is expected to be short- to intermediate-term in duration and to occur primarily by the dermal and inhalation routes. Exposure for workers mixing, loading and applying the product to greenhouse vegetables and ornamentals may be of long-term duration as crops are grown all year. However, the maximum number of applications are limited to three per year as part of an integrated pest management strategy.

Exposure estimates for mixers, loaders, applicators (M/L/A) are based on data from the Pesticide Handlers Exposure Database (PHED). PHED version 1.1 is a compilation of generic mixer/loader and applicator passive dosimetry data with associated software which facilitates the generation of scenario-specific exposure estimates. With a few exceptions, the PHED estimates meet criteria for data quality, specificity and quantity outlined under the North American Free Trade Agreement Technical Working Group on Pesticides. To estimate exposure for each use scenario, appropriate subsets of A and B (and C grade for low pressure handwand) were created from the liquid mixer/loader; aerial and groundboom applicator; and high pressure and low pressure handwand mixer/loader/applicator database files of PHED. All data were normalized for kg 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 which is most appropriate to the distribution of data for that body part. The confidence level is high for all scenarios except high and low pressure handwand for which the confidence level is low.

A crop grouping approach was used to derive handler exposure estimates using the maximum area treated per day for each crop group. The clothing scenario used to estimate mixer/loader, applicator exposure is a single layer of clothing and gloves for mixing and loading and for high and low pressure handwand mixing/loading and applying. For groundboom and aerial application, non-gloved data was used. Data was not available to assess application by chemigation; however, exposure is expected to be lower for this application method than by groundboom application.

Exposure and risk estimates for worker mixing/loading and applying Forbid 240 SC Insecticide/ Miticide to the proposed crop groups are summarized in Appendix I, Table 2. Based on a dermal absorption value of 3% target MOEs are achieved for all proposed scenarios.

Table 3.4.2.1.1 Summary of Exposure and Risk for Each Scenario

Crop/Scenario	Application Rate	Dermal Exposure (µg/kg bw/day)	Inhalation Exposure (µg/kg bw/day)	Combined MOE[1]
Greenhouse Application HP handwand MLA	0.012 kg a.i./100L	1.09	0.98	1060
Greenhouse Application LP handwand MLA	0.012 kg a.i./100L	0.00728	0.0116	116 000
Field crops Aerial ML	0.144 kg a.i./ha	1.55	1.61	696
Field crops Aerial APP	0.144 kg a.i./ha	0.292	0.0706	6070
Corn Groundboom Farmer MLA	0.144 kg a.i./ha	0.779	0.79	1400
Corn, Tuberous and Corm Vegetables Groundboom Custom MLA	0.144 kg a.i./ha	1.56	1.58	701
Leafy Greens, Brassica Leafy Vegetables, Cucurbits, Fruiting Vegetables Groundboom Farmer MLA	0.144 kg a.i./ha	0.166	0.169	6570
Leafy Greens, Brassica Leafy Vegetables, Cucurbits, Fruiting Vegetables Groundboom Custom MLA	0.144 kg a.i./ha	0.415	0.421	2630
Tuberous and Corm Vegetables Groundboom Farmer MLA	0.144 kg a.i./ha	0.415	0.421	2630
Strawberry Groundboom Farmer MLA	0.2784 kg a.i./ha	0.0502	0.0509	21800
Strawberry Groundboom Custom MLA	0.2784 kg a.i./ha	0.321	0.326	3400

ML = mixing/loading; APP = applying only; MLA = mixing/loading and applying , HP = high pressure, LP = low pressure

[1] Based on a NOAEL of 2.2 mg/kg bw/day from an oral multi-generation reproductive toxicity study. The target MOE is 300

3.4.2.2 Exposure and Risk for Workers Entering Treated Crops

For field crops, post-application exposure for workers entering fields treated with Forbid 240 SC Insecticide/Miticide is expected to be for an intermediate-term duration primarily by the dermal route. A tier one risk assessment was performed for workers entering field crops treated with two or three applications of Forbid 240 SC Insecticide/Miticide made 7 days apart based on a default value of 20% dislodgeable foliar residues and a 10% dissipation rate per day. A dermal absorption value of 3% was used and workers were assumed to be exposed for 8 hours per day.

A crop grouping approach was used to derive exposure estimates using the most conservative transfer coefficient for each crop group. With the proposed 12-hour re-entry interval (REI), target MOEs are achieved for all scenarios except one (Appendix I, Table 3). For hand harvesting and hand pruning Brassica Leafy vegetables (crop group 5) an REI of 2 days is required. This REI is considered economically feasible since the proposed PHI for this crop group is 7 days.

Table 3.4.2.2.1 Exposure and Risk Estimates for Workers Entering Treated Fields

Crop	Re-entry Activity	Application Rate (µg/cm^2)	Transfer Coefficient (cm^2/hour)	Exposure[1] (µg/kg bw/day)	MOE [2]
Field Corn	scouting	0.4257	1000	1.46	1510
Cucurbit Vegetables	hand harvesting, hand pruning and thinning, leaf pulling	0.4916	2500	4.21	522
Cucurbit Vegetables	scouting, weeding	0.4916	1500	2.53	870
Fruiting Vegetables	hand harvesting, hand pruning, staking, tying, thinning, training	0.4916	1000	1.68	1300
Fruiting Vegetables	scouting	0.4916	700	1.18	1860
Leafy Green Vegetables	hand harvesting, hand pruning, thinning	0.4916	2500	4.21	522
Leafy Green Vegetables	scouting	0.4916	1500	2.53	870
Leafy Green Vegetables	weeding	0.4916	500	0.843	2610
Brassica Leafy Vegetables	hand harvesting, hand pruning, topping, thinning, tying	0.4916	5000	8.43	261
Brassica Leafy Vegetables	scouting	0.4916	4000	6.74	326
Brassica Leafy Vegetables	weeding	0.4916	2000	3.37	653
Tuberous and	hand harvesting	0.4257	2500	3.65	603

Crop	Re-entry Activity	Application Rate (µg/cm^2)	Transfer Coefficient (cm^2/hour)	Exposure[1] (µg/kg bw/day)	MOE[2]
Corm Vegetables					
Tuberous and Corm Vegetables	scouting	0.4257	1500	2.19	1000
Tuberous and Corm Vegetables	weeding	0.4257	300	0.438	5020
Strawberry	hand harvesting, pinching, pruning, training	0.9505	1500	4.89	450
Strawberry	mulching, scouting, weeding	0.9505	400	1.3	1690

[1] Exposure = Application rate (µg/cm^2) × 10% dissipation × TC (cm^2/hr) × 8 hours × 3% dermal absorption/70 kg bw

[2] Based on a NOAEL of 2.2 mg/kg bw/day from an oral multi-generation reproductive toxicity study. The target MOE is 300

For greenhouse workers, exposure is expected to be of long-term duration, mainly by the dermal route by contacting treated foliage. Exposure estimates and margins of exposure for workers entering greenhouses to perform routine tasks on ornamental plants, cut flowers and greenhouse vegetables which have been treated with three applications of Forbid 240 SC Insecticide/Miticide are presented in Appendix I, Table 4. Exposure estimates are based on a default value of 20% dislodgeable foliar residues and no dissipation since no data was submitted to estimate foliar residue dissipation in greenhouses.

Table 3.4.2.2.2 Exposure and Risk Estimates for Greenhouse Workers Entering Treated Areas After Three Applications of Forbid 240 SC Insecticide/Miticide Made 7 or 10 Days Apart

Crop/Scenario	Transfer Coefficient (cm^2/hr)	Exposure[1] (mg/kg bw/day)	MOE[2]
Potted plants	400	0.000829	2650
Cut flowers - Hand Harvesting	2500	0.00517	425
Greenhouse Vegetables - Hand Harvesting	1800	0.0062	354

[1] Exposure = Application rate (µg/cm^2) × TC (cm^2/hr) × 8 hours × 3% dermal absorption/70 kg bw

[2] Based on a NOAEL of 2.2 mg/kg bw/day from an oral multi-generation reproductive toxicity study. The target MOE is 300

Target MOEs were achieved for workers entering treated areas to perform reentry activities on greenhouse ornamentals and greenhouse vegetables after three applications and are considered to be acceptable.

3.4.3 Residential Exposure and Risk

3.4.3.1 Handler Exposure and Risk

There are no domestic class products; therefore, a residential handler assessment was not required.

3.4.3.2 Postapplication Exposure and Risk

There are no domestic class products; therefore, a residential postapplication assessment was not required.

3.4.3.3 Bystander Exposure and Risk Assessment

Bystanders may be exposed to residues of Forbid 240 SC Insecticide/Miticide on strawberries at pick-your-own operations. This exposure is expected to be acute and to occur by the dermal and oral routes. There were no acute concerns for spiromesifen identified in the toxicological database, as such risk to bystanders at pick-your-own operations is considered to be acceptable.

3.5 Food Residues Exposure Assessment

3.5.1 Residues in Plant and Animal Foodstuffs

The residue definition for enforcement purposes is spiromesifen and BSN 2060-enol in primary crops and poultry matrices; and spiromesifen, BSN 2060-enol and BSN 2060-4-hydroxymethyl in rotational crops and ruminant matrices. The residue definition for risk assessment purposes in primary crops, rotational crops and ruminant matrices is spiromesifen, BSN 2060-enol and BSN 2060-4-hydroxymethyl; and spiromesifen, BSN 2060-enol, BSN 2060-4-carboxy-3-pentanol and BSN 2060-hydroxy-4-carboxy for poultry matrices. The data gathering and enforcement analytical methodologies, liquid chromatography with dual mass spectrometry (HPLC-MS/MS), is valid for the quantification of total spiromesifen residues in field crops (field corn, strawberry, leafy green vegetables, tuberous and corm vegetables, brassica leafy vegetables, cucurbit vegetables, fruiting vegetables); greenhouse vegetables (tomato, pepper and cucumber); and ruminant commodities (milk, ruminant fat, ruminant meat and ruminant meat byproducts). The total spiromesifen residues are stable in various plant commodities when stored in a freezer at $\leq -8°C$ for 541 days. Raw agricultural commodities were processed and residues were found to concentrate in dried tomatoes, tomato paste, tomato wet pomace, tomato puree, sugar beet molasses, wheat bran, wheat shorts and wheat middlings. Supervised residue trials conducted throughout the United States and Europe using an end-use product containing spiromesifen at either GAP or exaggerated rates in/on field corn, strawberry, leafy green vegetables, tuberous and corm vegetables, brassica leafy vegetables, cucurbit vegetables,

greenhouse cucumber, greenhouse tomato and greenhouse pepper are sufficient to support the proposed maximum residue limits.

3.5.2 Dietary Risk Assessment

Acute and chronic dietary risk assessments were conducted using the Dietary Exposure Evaluation Model (DEEM–FCID™, Version 2.0), which uses updated food consumption data from the United States Department of Agriculture's Continuing Surveys of Food Intakes by Individuals, 1994–1996 and 1998.

3.5.2.1 Chronic Dietary Exposure Results and Characterization

The following assumptions were made in a refined chronic analysis: default processing factors, median values for certain commodities and U.S. tolerances for all other commodities. The refined chronic dietary exposure from all supported spiromesifen food uses (alone) for the total population, including infants and children and all representative population subgroups is 38.5% (0.002698 mg/kg bw/day) of the ADI. The highest exposure and risk estimate for children 1–2 years old is 76.4% (0.005350 mg/kg bw/day) of the ADI. Aggregate exposure from food and water is considered acceptable. The PMRA estimates that chronic dietary exposure to spiromesifen from food and water is 43.5% (0.003046 mg/kg bw/day) of the ADI for the total population. The highest exposure and risk estimate is for children 1-2 years old at 83.8% (0.005867 mg/kg bw/day) of the ADI.

3.5.2.2 Acute Dietary Exposure Results and Characterization

No appropriate endpoint attributable to a single dose for the general population (including children and infants) was identified. Therefore no acute dietary exposure assessment was conducted.

3.5.3 Aggregate Exposure and Risk

The aggregate risk for spiromesifen consists of exposure from food and drinking water sources only; there are no residential uses. Aggregate risks were calculated based on chronic endpoints. There was no acute endpoint identified for the general population, including infants and children.

3.5.4 Maximum Residue Limits

Table 3.5.4.1 Proposed Maximum Residue Limits

MRLs (ppm)	Foods
0.2	Cucumber
0.02	Corn, field, grain
2	Strawberry
0.6	Tomato, paste
0.6	Tomato, cherry
2	Vegetable, brassica, head and stem, subgroup 5A
12	Vegetable, brassica, leafy greens, subgroup 5B
0.1	Vegetable, cucurbit, group 9, except cucumber
0.45	Vegetable, fruiting, group 8, except cherry tomato
12	Vegetable, leafy greens, subgroup 4A
0.02	Vegetable, tuberous and corm, subgroup 1C
0.03	Barley, grain
0.03	Wheat, grain,
0.03	Beet, sugar, roots
0.2	Beet, sugar, tops
0.05	Cattle, fat
0.01	Cattle, meat
0.05	Cattle, meat byproducts
0.05	Goat, fat
0.01	Goat, meat
0.05	Goat, meat byproducts
0.05	Horse, fat
0.01	Horse, meat
0.05	Horse, meat byproducts
0.05	Sheep, fat
0.01	Sheep, meat
0.05	Sheep, meat byproducts
0.005	Milk
0.1	Milk, fat

For additional information on MRLs in terms of the international situation and trade implications, refer to Appendix II.

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

4.0 Impact on the Environment

4.1 Fate and Behaviour in the Environment

Spiromesifen enters the soil in its use as an insecticide on vegetable and strawberry crops. Dissipation on soil is an important route of transformation. Under field conditions relevant to Canada, the half life is 4.5 days. BSN 2060-enol is a major transformation product, with a half life of 18 days. Under laboratory conditions, spiromesifen transforms moderately quickly, with half lives ranging from 2 to 18 days, depending on soil type and organic matter content. BSN 2060-enol transforms with half lives ranging from 15 to 63.6 days. Field and laboratory data indicate that spiromesifen is strongly bound to soil particles and is not expected to leach through the soil profile. Therefore, spiromesifen is not expected to enter groundwater. The major transformation product, BSN 2060-enol is expected to leach through the soil profile and therefore expected to enter groundwater.

Spiromesifen could reach water systems by spray drift or runoff. It is not soluble in water, therefore, transport is likely to occur when bound residues are carried to surface water through runoff. Dissipation in water is an important route of transformation, with half lives ranging from 3.6 to 48 days. In both aerobic and anaerobic water/sediment systems, spiromesifen readily binds to sediment where it transforms with a half life ranging from 4.1 to 18 days. The major transformation product, BSN 2060-enol is soluble in water and therefore partitions into the water column, where its rate of transformation is slow (half life greater than 120 day study duration).

Its vapour pressure and Henry's law constant are so low that spiromesifen is considered to be non-volatile in the environment. Therefore, spiromesifen residues are not expected in the air and long-range transport is not expected.

Data on the fate and behaviour of spiromesifen and its major transformation products are summarized in Table 7 of Appendix I.

4.2 Effects on Non-Target Species (Appendix I, Table 8)

To estimate risk of potential adverse effects on non-target species, a quotient method is used. The risk quotient (RQ) is calculated by dividing the exposure estimate by a value representing a toxicity endpoint. A screening-level risk assessment is initially performed using the estimated environmental concentrations (EECs) for a worst-case scenario (e.g. direct overspray of a body of water) and the most sensitive toxicity endpoint. Low risk is predicted if the risk quotient is less than the trigger value of one. In these cases, no further assessment is done. For those groups of organisms for which the RQ is greater than one, a refined assessment is undertaken. A refined assessment takes into consideration more realistic exposure scenarios (e.g. drift to non-target habitats and runoff to water bodies) and may consider different toxicity endpoints.

4.2.1 Effects on Terrestrial Organisms

Risk of spiromesifen to terrestrial organisms was based upon evaluation of toxicity data for the following:

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

For terrestrial vertebrates spiromesifen did not cause mortality on an acute (gavage) or short-term dietary basis. Sublethal effects (thyroid, kidney, spleen and cholesterol effects at 80 mg/kg bw/day for mice and 500 mg/kg bw/day for rats) were observed in small mammals. Observable reproductive effects were reported following long-term exposure of birds (reduced number of eggs laid, increased number of eggs cracked, reduced number of fertile embryos and hatching success at 228 mg a.i./kg diet; reduced adult male body weight at 681 mg a.i./kg diet) and small mammals (offspring effects at 120 mg a.i./kg diet). Risk quotients calculated under a realistic worst-case scenario exceeded the trigger value of one for birds and mammals exposed to food contaminated with spiromesifen on the field of application (Appendix I, Table 9).

For terrestrial invertebrates, spiromesifen was not toxic in acute dose response studies, with LC_{50} values exceeding the highest dose (limit) tested for earthworms. However, mortality was observed in bees exposed to Spiromesifen Technical Insecticide/Miticide at 200 µg a.i./bee; and Forbid 240 SC Insecticide/ Miticide at 49.5 µg a.i./bee. Mortality was also observed in three (*Coccinella septempunctata*, *Typhlodromus pyri* and *Aphidius rhopalosiphi*) of the six predator and parasite species tested. The rate at which Forbid 240 SC Insecticide/Miticide caused mortality ranged from 9.8 to 64.8 g a.i./ha with aphid parisitoids being the most sensitive. Reproductive impairment was also observed in *Coccinella septempunctata* and *Aphidius rhopalosiphi* at 23 and 2.2 g a.i./ha. Risk quotients calculated under a realistic worst-case scenario exceeded the trigger value of one for predator and parasites exposed to food contaminated with spiromesifen on the field of application (Appendix I, Table 9).

Multiple refined assessments were conducted. The first assessment considered that the most likely scenario of exposure to birds, mammals and terrestrial beneficial insects would incorporate a foliar dissipation rate of 10 days compared to 35 days. The 35 day default foliar half life is based on a data set of 447 foliar half-life estimates acquired from an extensive literature review (Willis and McDowell, 1987). Among this data set, 93% of the half-lives reported were less than 10 days and 76% were less than 5 days. Since spiromesifen is not persistent in/on other media, a refined foliar dissipation rate of 10 days was included for assessment. Based on a refined foliar dissipation half life of 10 days, the risk quotient still exceeded the trigger value of one for birds, mammals and terrestrial beneficial insects. The second assessment considered the potato and corn application rate for spiromesifen. The 834 g a.i./ha application rate is for strawberries which has a low crop area (3359 ha) compared to field corn and potato use (1 224 900 and 63 862 ha, respectively) at a cumulative rate of 288 g a.i./ha. Since the majority of exposure to birds, mammals and terrestrial beneficial insects from

contaminated food sources will result from use on these latter two crops, a refined assessment was conducted to evaluate this risk. The risk quotient did not exceed the trigger value for birds and for mammals it would require 69 to 85% of the mammal's diet to be contaminated with spiromesifen to result in an RQ of one for dietary effects. As spiromesifen is not persistent in the environment, such an exposure is not expected under field conditions and thus, the chronic risk to small mammals is not a concern. For terrestrial beneficial insects the risk quotient still exceeded the trigger value of one. Since the risk quotient exceeded a value of one and the mortality in both ladybird beetles and predaceous mites was greater than 80% under laboratory conditions, a toxicity advisory statement was added to the label.

An off-field assessment for birds and mammals was also considered. This scenario assumed that the most likely scenario of exposure to food contaminated with spiromesifen is through drift (Appendix I, Table 9). A refined estimated environmental concentration (EEC) was calculated based on the percent deposition at one metre downwind according to the EAD ground application model. This model is based on the data of Wolf and Caldwell (2001) and predicts percent deposit at one metre to be 11% for a fine spray quality. Based on the off-field assessment, risk quotients did not exceed the trigger value of one for birds and mammals exposed to spiromesifen contaminated food sources (Appendix I, Table 11).

For terrestrial plants, seedling emergence and vegetative vigour were examined. However, spiromesifen (Forbid 240 SC Insecticide/Miticide) affected only vegetative vigour. Between the three endpoints used to assess vegetative vigour (height, dry weight and phytotoxicity), dry weight was the most sensitive endpoint. The rate at which spiromesifen negatively affected the vegetative vigour of 25% of the population was 27 g a.i./ha. The highest cumulative application rate is 835 g a.i./ha. Risk quotients calculated under a realistic worst-case scenario exceeded the trigger value for one monocotyledonous species (ryegrass) and one dicotyledonous species (turnip) (Appendix I, Table 9).

A refined assessment considered that the most likely scenario of exposure to non-target plants is through drift (Appendix I, Table 4). For the monocotyledonous and dicotyledonous species, rates as low as 3.2% and 6.8% of the application rate is expected to affect vegetative vigour (EC_{25} divided by application rate), respectively. Fractions this low can be expected to drift to adjacent habitats. Therefore, using drift deposition data from Canadian field trials, a ground buffer zone of 1 to 2 metres and an aerial buffer zone of 40 to 45 metres (depending on crop) was calculated to protect sensitive non-target plant species in adjacent habitats. The buffer zone is also a function of the EC_{25} of the most sensitive plant tested.

4.2.2 Effects on Aquatic Organisms

Risk of Spiromesifen Technical Insecticide/Miticide and/or Forbid 240 SC Insecticide/Miticide and/or BSN 2060-enol to freshwater aquatic organisms was based upon evaluation of toxicity data (Appendix I, Table 8) for the following:

- two invertebrates; daphnid (acute and long-term exposure) and chironomid (long-term exposure)
- three fish species (acute and long-term exposure)
- amphibian species using fish as a surrogate
- one algae and one vascular plant

Risk of spiromesifen to marine aquatic organisms was based upon evaluation of toxicity data for the following:

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

Spiromesifen Technical Insecticide/Miticide: For freshwater and marine invertebrates, spiromesifen did not cause acute mortality. Observable reproductive effects were reported for daphnid following long-term exposure (reduced neonate production at 0.45 µg a.i./L). Reduced emergence and reduced developmental rates were observed for sediment dwelling chironomid at 0.01 µg a.i./L. For freshwater aquatic vertebrates, spiromesifen caused acute mortality in fish at concentrations ranging from 13.3 to 40.1 µg a.i./L, depending on species, with rainbow trout being the most sensitive species tested. Observable reproductive effects were reported following long-term exposure (reduced hatching success at 3.0 µg a.i./L to 18.4 µg). Using the most sensitive fish species as a surrogate for amphibians, effects on survival and reproduction would be expected at concentrations of 13.3 and 3.0 µg a.i./L, respectively. For marine vertebrates, no acute or chronic effects were observed. For algae, spiromesifen caused a reduction in growth at 6.8 µg a.i./L. No effects were observed for the vascular plant, *Lemna gibba*. Risk quotients calculated under a realistic worst-case scenario exceeded the trigger value of one for freshwater and marine invertebrates and vertebrates, algae, amphibians and vascular plants exposed to spiromesifen (Appendix I, Table 10).

Forbid 240 SC Insecticide/Miticide (end use product): For aquatic invertebrates, exposure to Forbid 240 SC Insecticide/Miticide at 0.26 mg a.i./L did result in acute mortality. Observable reproductive effects were reported following long-term pulse exposure (reduced neonate production and extended time to brood at 4.8 µg a.i./L). Daphnid population numbers were also reduced at 0.56 µg a.i./L following long-term pulse exposure. Risk quotients calculated under a realistic worst-case scenario exceeded the trigger value of one for invertebrates chronically exposed to Forbid 240 SC Insecticide/Miticide (Appendix I, Table 10). For aquatic vertebrates, Forbid 240 SC Insecticide/Miticide caused acute mortality in fish at concentrations ranging from 34 to 104 µg a.i./L, with bluegill being more sensitive than the rainbow trout. Sublethal effects were also observed at the lowest concentration tested for bluegill sunfish (7.6 µg a.i./L). Long-term reproduction studies were not conducted with the end use product. Risk quotients

calculated under a realistic worst-case scenario exceeded the trigger value of one for invertebrates exposed to Forbid 240 SC Insecticide/Miticide (Appendix I, Table 10).

BSN 2060-enol (transformation product): For invertebrates and vertebrates, exposure to BSN 2060-enol did not cause acute mortality, or long-term effects on reproduction. Algae was the only species affected by BSN 2060-enol, with reduced growth observed at 6.2 µg a.i./L. Risk quotients calculated under a realistic worst-case scenario did not exceed the trigger value of one for aquatic organisms exposed to BSN 2060-enol, except for algae (Appendix I, Table 10).

Two refinements were conducted, the first considered that the most likely routes of entry of Spiromesifen Technical Insecticide/Miticide or Forbid 240 SC Insecticide/Miticide into water are through drift (Appendix I, Table 4). A refined EEC was calculated based on the percent deposition at one metre downwind according to the EAD ground application model. This model is based on the data of Wolf and Caldwell (2001) and predicts percent deposit at one metre to be 11% for a fine spray quality. Based on this assessment, risk quotients still exceeded the trigger value of one for freshwater invertebrates and freshwater and marine vertebrates exposed to spiromesifen and Forbid 240 SC Insecticide/Miticide. Therefore, using drift deposition data from Canadian field trials, a ground buffer zone of 2 to 10 metres for freshwater habitat and 1 to 2 metres for marine habitat; and an aerial buffer zone of 25 to 350 metres for freshwater habitat and 1 to 10 for marine habitat (depending on crop) was calculated to protect sensitive aquatic species in adjacent habitats. The buffer zone is also a function of the most sensitive species tested.

The second refinement considered that the most likely routes of entry of Spiromesifen Technical Insecticide/Miticide or Forbid 240 SC Insecticide/Miticide into water are through runoff (Appendix I, Table 12). Estimated environmental concentrations of spiromesifen for a Level 1 receiving water body runoff scenario for aquatic risk assessment were simulated using the PRZM/EXAMS models. This water body consists of a one hectare wetland with an average depth of 0.8 m and a 10 ha drainage area. Based on this assessment, risk quotients did not exceed the trigger value of one for freshwater invertebrates and freshwater and marine vertebrates exposed to spiromesifen or Forbid 240 SC Insecticide/Miticide, however, the risk quotient was still exceeded for algae exposed to BSN 2060-enol (Appendix I, Table 13). To mitigate this risk, a surface water advisory statement was added to the label.

5.0 Value

5.1 Effectiveness Against Pests

Data from 42 efficacy studies (small plot and greenhouse) conducted between 1997 and 2005 in Mexico, the United States and Europe (greenhouse) were reviewed. Trials were not reviewed when pest pressure was too low to provide an adequate determination of efficacy. Trials were conducted in the United States from Florida to California and as far north as Oregon, Washington and Nebraska. For each trial, an appropriate experimental design was employed, which included an untreated control and an active ingredient that was considered as an industry standard.

Control of individual insect species was assessed and compared to an untreated control. Observations were made at various times throughout the growing season after treatment(s) occurred.

5.1.1 Acceptable Efficacy Claims

5.1.1.1 Foliar applications of Forbid 240 SC Insecticide/Miticide

The reviewed efficacy data support the concentrations and rates outlined in Table 5.1.1.1. No distinct rate effect was demonstrated. Any differences between the rate for a pest on different crops can be accounted for by increased or reduced water volume.

Table 5.1.1.1 Use claims for Forbid 240 SC Insecticide/Miticide

Insects Controlled	Insecticide Rate or Concentration
Two-spotted spider mite and whiteflies on greenhouse vegetables (tomatoes, pepper and cucumber)	0.3–0.5 mL product/L (0.072–0.12 g a.i./ha)
Two-spotted spider mite and whiteflies on greenhouse ornamentals	0.03 mL product/ha (0.072 g a.i./ha)
Two spotted spider mite, broad mites and whiteflies on outdoor ornamentals	0.03 mL product/ha (0.072 g a.i./ha)
Two spotted spider mite and banks grass mite on field corn	400–600 mL product/ha (96–144 g a.i./ha)
Two spotted spider mite and whiteflies on cucurbit vegetables (crop group 9) and tuberous and corm vegetables (crop group 1C)	500–600 mL product/ha (120–144 g a.i./ha)
Two spotted spider mite, broad mite and whiteflies on fruiting vegetables (crop group 8)	500–600 mL product/ha (120–144 g a.i./ha)
Whiteflies on leafy green (crop group 4A) and brassica leafy vegetables (crop group 5)	500–600 mL product/ha (120–144 g a.i./ha)
Strawberries	880–1160 mL product/ha (211–278 g a.i./ha)

5.1.1.2 Insecticide Tank Mix Combinations

Tank mixes with Forbid 240 SC Insecticide/Miticide were not proposed or assessed.

5.2 Phytotoxicity to Host Plants

Non-safety adverse effects were summarized for field trials conducted in North America and greenhouse trials conducted in Europe. In the field, Forbid 240 SC Insecticide/Miticide does not impact the visual appearance of broccoli, cantaloupe, corn, cucumber, eggplant, potato, rose or strawberry when rates as high as 300 g a.i./ha were applied three times throughout the season. In the greenhouse, the same product does not impact the visual appearance of tomato, eggplant,

carnation, chrysanthemum, gerbera, or Hedera helix, however, data on rose and cucumber were less definitive. When trials were conducted in the winter, crop injury on cucumber was described as thinning of leaf margins and leaf curling; however, despite this observable damage, the level of toxicity was rated as acceptable. Trials repeated in the summer had no measurable damage. Leaf curl on greenhouse roses remained at acceptable levels and was transitory.

5.2.1 Acceptable Claims for Host Plants

Only greenhouse roses and cucumber experienced any non-safety adverse effects when treated with rates higher than those recommended. The adverse effects were also considered acceptable or transitory in nature. Despite the lack of phytotoxic effects on crops other than greenhouse roses and cucumber, all species and varieties of crops listed on the label have not been evaluated. It is recommended to test Forbid 240 SC Insecticide/Miticide on a small scale basis before full commercial use.

5.3 Impact on Succeeding Crops

The impact on succeeding crops was not evaluated in this submission.

5.3.1 Acceptable Claims for Rotational Crops

The impact on rotational crops was not evaluated in this submission.

5.4 Economics

Mites and whiteflies are predominant pests in warm, dry environments. As such, Forbid 240 SC Insecticide/Miticide will have limited use in the field simply because the Canadian climate does not favour these pests. Despite this, the largest field use will be in strawberries where mites are a common pest. However in greenhouses, mites and whiteflies are persistent perennial pests with the potential of causing considerable damage to crops. Losses in the greenhouse industry would be due to unmarketable fruit, vegetables, or ornamentals and reduced yields. Exact economic losses are not available, but would vary with the pest and value of the crop under consideration.

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 classes of insecticides include the synthetic pyrethroids and neonicotinoids, as well as growth regulators, avermectins, juvenile hormone analogs and unclassified actives, such as soap, oil and sulphur. The major alternatives currently registered for control of mites and whiteflies on the labelled crops are listed in Appendix I, Table 14.

Spiromesifen belongs to the class of insecticides known as inhibitors of lipid synthesis (resistance management group 23). There is one active ingredient from this resistance

management group, spirodiclofen, currently registered for control of mites in pome and stone fruit and grapes in Canada. Spiromesifen, which is to be used on greenhouse and field vegetables and strawberries, belongs to a new group of insecticides and therefore, provides an active ingredient with a new mode of action for resistance management.

5.5.2 Compatibility with Current Management Practices Including Integrated Pest Management

Forbid 240 SC Insecticide/Miticide is compatible with current management practices. These products can be applied with conventional application equipment used for field vegetables, strawberries and greenhouses. As well, it can be applied with currently used aerial application equipment for all outdoor field uses (except ornamentals). Growers are familiar with the monitoring techniques used to determine if and when applications are needed. The new mode of action of this end-use product offers growers an alternative to rotate with currently registered chemicals.

The effect of Forbid 240 SC Insecticide/Miticide on beneficial/predacious insects and mites is unclear. Additional information is needed to determine if this product is safe for use in biological control programs, such as those prevalent in greenhouse production.

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

Repeated use of insecticides having the same mode of action in a control program increases the probability of naturally selecting the biotypes, a group of insects within a species that has biological traits that are not common to the population as a whole, with less susceptibility to insecticides of the same mode of action. Therefore, Forbid 240 SC Insecticide/Miticide should be used in rotation with insecticides that have different modes of action.

The Forbid 240 SC Insecticide/Miticide label includes 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

Spiromesifen is the first resistance management group 23 active ingredient registered for use on field vegetables and ornamentals, strawberries and greenhouse ornamentals and vegetables. This will provide a new active ingredient for resistance management. As well, some of the registered broad spectrum active ingredients, such as the organophosphates, organochlorines and the carbamates, are under re-evaluation and may no longer be available in the future.

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, spiromesifen 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 spiromesifen were also considered, including major transformation products formed in the environment, microcontaminants in the technical product, Spiromesifen Technical Insecticide/Miticide and formulants in the end-use product, Forbid 240 SC Insecticide/Miticide. The PMRA has reached the following conclusions:

- Based on experimental data, spiromesifen does not meet the criteria for persistence. Its values for half-life in water (≤2 days), soil (≤35 days) and sediment (≤39 days) are below the TSMP Track-1 cut-off criteria for water (≥182 days), soil (≥182 days) and sediment (≥365 days). The vapour pressure (5.7×10^{-8} mm Hg or 7×10^{-6} Pa) and Henry's law constant (1.9×10^{-7} atm·m^3/mole) for spiromesifen indicate that volatilization is not an important route of dissipation, thus long-range atmospheric transport is not likely to occur. Spiromesifen does not meet the criteria for bioaccumulation. The bioconcentration factor (BCF) of spiromesifen in whole fish is 916, which is below the TSMP Track-1 cut-off criterion of BCF ≥5000. The octanol-water partition coefficient (log P_{ow}) for BSN 2060-enol is 0.2, which is below the TSMP Track-1 cut-off criterion of ≥5.0.

- Spiromesifen does not form any major transformation products in the environment that meet all TSMP Track-1 criteria. The half-life of BSN 2060-enol in soil (61.9 days) is below the TSMP Track-1 cut-off criterion (≥182 days). In the aquatic environment BSN 2060-enol is persistent (based on parent fate studies) and may exceed 182 days.

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

Spiromesifen Technical Insecticide/Miticide 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 product, Forbid 240 SC Insecticide/Miticide Insecticide, does 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*.

7.0 Summary

7.1 Human Health and Safety

The toxicology database submitted for spiromesifen is adequate to define the majority of toxic effects that may result from human exposure to spiromesifen. In subchronic and chronic studies on laboratory animals, target organs included the spleen, liver, uterus, thyroid gland and adrenal gland. There was no evidence of carcinogenicity. There was evidence of increased susceptibility of the young in a reproductive toxicity study. Spiromesifen is not considered to be a neurotoxicant.

Mixer, loader, applicators and workers entering treated fields and greenhouses are not expected to be exposed to levels of spiromesifen that will result in unacceptable risk when Forbid 240 SC Insecticide/Miticide is used according to label directions. The personal protective equipment on the product label is adequate to protect workers and no additional personal protective equipment is required.

The nature of the residue in plants and animals is adequately understood. The residue definition for enforcement purposes is spiromesifen and BSN 2060-enol in primary crops and poultry matrices and spiromesifen, BSN 2060-enol and BSN 2060-4-hydroxymethyl in rotational crops and ruminant matrices. The proposed use of spiromesifen on field corn, strawberry, leafy green vegetables, tuberous and corm vegetables, *brassica* leafy vegetables, cucurbit vegetables, fruiting vegetables, greenhouse cucumber, greenhouse tomato and greenhouse pepper does not constitute an unacceptable chronic 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. The PMRA recommends that the following maximum residue limits be specified under the authority of the *Pest Control Products Act*:

Cucumber (0.20 ppm)
Tomato, cherry (0.6 ppm)
Corn, field, grain (0.02 ppm)
Strawberry (2 ppm)
Tomato, paste (0.6 ppm)
Vegetable, brassica, head and stem, subgroup 5A (2 ppm)
Vegetable, brassica, leafy greens, subgroup 5B (12 ppm)
Vegetable, cucurbit, group 9 (except cucumbers) (0.1 ppm)
Vegetable, fruiting, group 8 (except cherry tomatoes) (0.45 ppm)
Vegetable, leafy greens, subgroup 4A (12 ppm)
Vegetable, tuberous and corm, subgroup 1C (0.02 ppm)
Barley, grain (0.03 ppm)

Wheat, grain (0.03 ppm)
Beet, sugar, roots (0.03 ppm)
Beet, sugar, tops (0.2 ppm)
Fat of cattle, sheep, goat, horse (0.05 ppm)
Meat of cattle, sheep, goat, horse (0.01 ppm)
Meat byproducts of cattle, sheep, goat, horse (0.05 ppm)
Milk (0.005 ppm)
Milk, fat (0.1 ppm)

7.2 Environmental Risk

Spiromesifen presents a low risk to wild mammals, birds, earthworms and bees. However, spiromesifen does pose a risk to freshwater aquatic invertebrates, freshwater and marine vertebrates, terrestrial plants and beneficial insects. Therefore, ground buffer zones of 2 to 10 metres (depending on crop and spray technology) for freshwater habitats, 1 metre for marine habitats and 1 to 2 metres for terrestrial habitats; and aerial buffer zones of 25 to 350 metres for freshwater habitats, 1 to 10 for marine habitats and 40 to 45 metres for terrestrial habitats were calculated to protect sensitive aquatic species and non-target plant species in adjacent habitats. Toxicity advisory statements were also added to the label.

7.3 Value

The data submitted to register Forbid 240 SC Insecticide/Miticide are adequate to describe its efficacy for use in field vegetables, greenhouse ornamentals and vegetables (tomato, pepper and cucumber), outdoor ornamentals and strawberries. Forbid 240 SC Insecticide/Miticide controls whiteflies (including sweet potato, silverleaf and greenhouse) and selected mites (two spotted spider mite, broad mite and Banks grass mite). Tolerance to Forbid 240 SC Insecticide/Miticide is acceptable though caution should be exercised when treating ornamentals as not all species and varieties have been tested. Forbid 240 SC Insecticide/Miticide provides an alternative to currently registered organophosphate, carbamate and organochlorine insecticides. Spiromesifen provides a new mode of action (group 23) for use on the labelled crops, which will help resistance management.

7.4 Unsupported Uses

Certain uses originally proposed by the applicant are not supported by the PMRA because value has not been adequately demonstrated. Unsupported uses are outlined in Table 15 of Appendix I.

8.0 Regulatory Decision

Health Canada's PMRA, under the authority of the *Pest Control Products Act* and in accordance with the Pest Control Products Regulations, has granted conditional registration for the sale and use of the technical grade active ingredient Spiromesifen Technical Insecticide/Miticide and the end-use product Forbid 240 SC Miticide/Insecticide to control mites and whiteflies on greenhouse and outdoor ornamentals, greenhouse and field vegetables as well as strawberries. An evaluation of current scientific data from the applicant, scientific reports and information from other regulatory agencies has resulted in the determination that, under the proposed conditions of use, the end-use product has value and does not present an unacceptable risk to human health or the environment.

Although the risks and value have been determined to be acceptable when all risk-reduction measures are followed, as a condition of these registrations, additional scientific information is being requested from the registrant as a result of this evaluation (see below).

Human Health

The following additional data is requested for the assessment of dietary risk:

- Storage stability data for the commodities analysed in the Field Accumulation in Rotational Crops studies to validate the 22-month storage intervals.

List of Abbreviations

µg	micrograms
1/n	exponent for the Freundlich isotherm
a.i.	active ingredient
ADI	acceptable daily intake
ALS	acetolactate synthase
ARfD	acute reference dose
atm	atmospheres
bw	body weight
CAS	chemical abstracts service
cm	centimetres
DACO	data code
DF	dry flowable
DNA	deoxyribonucleic acid
EC_{25}	effective concentration on 25% of the population
EEC	estimated environmental concentration
g	gram
ha	hectare(s)
HDT	highest dose tested
Hg	mercury
HPLC	high performance liquid chromatography
ILV	independent laboratory validation
IUPAC	International Union of Pure and Applied Chemistry
kg	kilogram
K_d	soil-water partition coefficient
K_F	Freundlich adsorption coefficient
km	kilometre
K_{oc}	organic-carbon partition coefficient
K_{ow}	*n*–octanol-water partition coefficient
L	litre
LC_{50}	lethal concentration 50%
LD_{50}	lethal dose 50%
LOAEL	lowest observed adverse effect level
LOEC	low observed effect concentration
LOQ	limit of quantitation
LR_{50}	lethal rate 50%
mg	milligram
mL	millilitre
MAS	maximum average score
MOE	margin of exposure
MRL	maximum residue limit
MS	mass spectrometry
m/z	mass to charge ratio
N/A	not applicable
NOAEL	no observed adverse effect level
NOEC	no observed effect concentration

NOEL	no observed effect level
NOER	no observed effect rate
N/R	not required
NZW	New Zealand white
OC	organic carbon content
OM	organic matter content
PBI	plantback interval
PHI	preharvest interval
p*K*a	dissociation constant
PMRA	Pest Management Regulatory Agency
ppm	parts per million
REI	re-entry interval
R/F	residue-to-feed ratio
RSD	relative standard deviation
SC	soluble concentrate
$t_{1/2}$	half-life
T3	tri-iodothyronine
T4	thyroxine
TBC	thyroxine binding capacity
TRR	total radioactive residue
TSH	thyroid stimulating hormone
TSMP	Toxic Substances Management Policy
UAN	urea ammonium nitrate
UF	uncertainty factor
USEPA	United States Environmental Protection Agency
UV	ultraviolet
v/v	volume per volume dilution

Appendix I Tables and Figures

Table 1 Residue Analysis

Matrix	Method ID	Analyte	Method Type	LOQ		Reference
Plant	00631 (data-gathering); 00631/M001 (enforcement)	BSN 2060, BSN 2060-enol	HPLC-MS/MS[1]	0.01 ppm	broccoli (head and plant), bean, corn (grain, green material, straw), cottonseed, cucumber fruit, pepper fruit, melon (fruit, pulp, peel), strawberry (fruit, jam, preserves), sugar beet (root, leaf), tomato (fruit, juice, preserve, puree)	PMRA ID1296208, 1296209, 1296272, 1330048 MRID 45854503, 45819506, 45854504, 45819421.
Animal	110878 (data gathering and enforcement)	BSN 2060, BSN 2060-enol, BSN 2060-4-hydroxymethyl	HPLC-MS/MS[1]	0.01 ppm	bovine muscle, bovine fat	PMRA ID 1296207, 1296271, 1330047 MRID 45819416, 45819410, 45819423
				0.05 ppm	bovine kidney, bovine liver	
				0.005 ppm	milk	
Rotational crops	110333	BSN 2060-4-hydroxymethyl, BSN 2060-4-hydroxymethyl glucoside	HPLC-MS/MS[2]	0.01 ppm	-wheat RAC (forage, grain); -wheat processed commodities (bran, flour, germ, middlings, shorts); -barley grain	PMRA ID 1296206, 1296294, 1296204 MRID 45819413, 45819422, 45819505;
				0.02 ppm	-wheat RAC (hay, straw); -alfalfa (forage, hay); -barley (hay, straw); -sugar beets (tops, roots); - turnips (tops, roots)	PMRA ID 1296206, 1296294, 1296204 MRID 45819413, 45819422, 45819505;

Matrix	Method ID	Analyte	Method Type	LOQ	Reference
Soil	715	Spiromesifen (BSN 2060)	HPLC-MS/MS 371 to 273 m/z	10 ppb	1296709
		BSN 2060-enol	HPLC-MS/MS 273 to 255 m/z		
	Not specified	BSN 2060-4-carboxy	HPLC-MS/MS 301 to 195 m/z	10 ppb	1344176
		BSN 2060-cyclobytyl photoisomer	HPLC-MS/MS 371 to 209 m/z		
		BSN-enol photoisomer	HPLC-MS/MS 255 to 209 m/z		
Sediment	The method submitted for soil was extended to sediment				
Water	650	Spiromesifen (BSN 2060)	HPLC-MS/MS 371 to 273 m/z	0.05 ppb	1296697
		BSN 2060-enol	HPLC-MS/MS 273 to 255 m/z		

[1] Spiromesifen (BSN 2060) transitions: 371 to 273 or 276 m/z
[2] BSN 2060-enol transitions: 273 to 187 m/z
[3] BSN 2060-4-hydroxymethyl transitions: 287 to 207 m/z

Table 2 Acute Toxicity of Spiromesifen Technical Insecticide/Miticide (BSN 2060) and Its Associated End-Use Product (Forbid 240 SC Insecticide/Miticide)

Study Type	Species	Result	Comment	Reference
Acute Toxicity of Spiromesifen Technical/Insecticide				
Oral	Rat	LD_{50} > 2000 mg/kg bw	LOW TOXICITY	1296732
Dermal	Rat	LD_{50} > 2000 mg/kg bw	LOW TOXICITY	1296736
Inhalation	Rat	LC_{50} > 4.87 mg/L	LOW TOXICITY	1296606
Skin irritation	Rabbit	MAS[a] = 0	Non-irritating	1296730
Eye irritation	Rabbit	MAS = 0	Non-irritating	1296731
Skin sensitization (maximization)	Guinea pig	Positive	Potential dermal sensitizer	1296725
Acute Toxicity of End-Use Product—Forbid 240 SC Insecticide/Miticide				
Oral	Rat	LD_{50} > 2000 mg/kg bw	LOW TOXICITY	1296250
Dermal	Rat	LD_{50} > 4000 mg/kg bw	LOW TOXICITY	1296228
Inhalation	Rat	LC_{50} > 1.52 mg/L	SLIGHT TOXICITY	1296228
Skin irritation	Rabbit	MAS = 0	Non-irritating	1296225
Eye irritation	Rabbit	MAS = 0	Non-irritating	1296226
Skin sensitization (Buehler)	Guinea pig	Negative	Non-sensitizing	1296227

[a] MAS = maximum average score for 24, 48 and 72 hours

Table 3 Toxicity Profile of Spiromesifen Technical Insecticide/Miticide

Study Type	Species	Results[a] (mg/kg/day)	Reference
28-day dermal	Rat	**NOAEL:** 1000 mg/kg bw/day, the highest dose tested. **LOAEL:** Not established as no adverse effects were noted.	1296609
5-day inhalation	Rat	A NOAEL and LOAEL were not established as this was a dose range-finding study and was considered supplemental. No adverse effects were noted at 0.08 mg/L (20.7 mg/kg bw/day). The following adverse effects were noted at the next highest concentration of 0.5 mg/L (134 mg/kg bw/day): mortality (F), clinical signs, abnormal reflexes, body weight loss, reduced body temperature, decreased platelet count (F), increased clotting time (F), increased serum liver enzymes (F), decreased serum triglycerides (M), increased relative lung weight, decreased absolute and relative spleen weight, dark red foci in the lung (M), lung “less collapsed”, small thymus and spleen, pale spleen and liver (F), bloated stomach (F), white viscous content in the trachea and nasal cavity (F).	1296659
28-day inhalation	Rat	**NOAEL:** 0.081 mg/L (21.1 mg/kg bw/day), the highest dose tested. **LOAEL:** Not established as no adverse effects were noted.	1325487
28-day dietary	Mouse	A NOAEL and LOAEL were not established as this was a dose range-finding study and was considered supplemental. At 7000 ppm (1292/1706 mg/kg bw/day in M/F), the following effects were noted: mortality, body weight loss, reduced water consumption, dark red lungs, fluid-filled stomach.	1296605

Study Type	Species	Results[a] (mg/kg/day)	Reference
28-day dietary	Rat (M only)	**NOAEL (M):** Not established as only one dose was tested. **LOAEL (M):** 444 mg/kg bw/day; clinical signs (clonic saltatory spasms, laboured breathing, lacrimation, piloerection, vocalization, uncoordinated gait); reduced food consumption, body weight and body weight gain; increased neutrophils, monocytes and basophils; decreased platelet count and increased clotting time; increased serum liver enzymes (ALAT, ASAT, ALK); decreased glucose, cholesterol, triglycerides, creatinine, protein, albumin, sodium, calcium and phosphorus in the blood; increased liver tissue enzymes (N-DEM, O-DEM); increased relative testes weight, decreased absolute and relative thymus weight; lipid vacuolation of enterocytes in the duodenum and jejunum; cytoplasmic basophilia in periportal hepatocytes; hypertrophy of thyroid follicular cells; colloidal vacuoles in thyroid; hypocellularity in the periarteriolar lymphocyte sheaths of the spleen; reduction in the medullary area of the thymus, decreased number of lymphocytes in the cortex and medulla of the thymus; abnormal germ cells in the testes; focal foam cell infiltration in the lung.	1296735
28-day dietary	Rat (F only)	**NOAEL (F):** 10.9 mg/kg bw/day. **LOAEL (F):** 53.4 mg/kg bw/day; increased liver tissue enzymes (ALD, EH), decreased cholesterol and triglycerides in the blood, decreased mitogen stimulation in the spleen, increased cell proliferation in the liver and the renal medulla, increased nuclear size in the liver, thyroid follicular cell hypertrophy.	1296726
29-day dietary	Dog	A NOAEL and LOAEL were not established as this was a dose range-finding study and was considered supplemental. At 3.7/3.9 mg/kg bw/day in M/F, slight increases in serum ALK and T4 was descreased as well as liver tissue enzymes (N-DEM, O-DEM, ECOD, ALD, EH) were noted.	1296535
90-day dietary	Mouse	**NOAEL:** Not established as effects were noted at the lowest dose tested. **LOAEL:** 21.7/35.3 mg/kg bw/day in M/F; decreased hemoglobin (F), decreased cholesterol, discoloured adrenal glands, cytoplasmic eosinophilia in the zona fasciculata of the adrenal gland, decreased fine vesiculation of the adrenal gland.	1296607

Study Type	Species	Results[a] (mg/kg/day)	Reference
90-day dietary Conducted to determine NOAEL.	Mouse	**NOAEL (M):** 11.5 mg/kg bw/day, the highest dose tested. **NOAEL (F):** 5.1 mg/kg bw/day. **LOAEL (M):** Not established as no adverse effects were noted. **LOAEL (F):** 20.3 mg/kg bw/day; decreased cholesterol, cytoplasmic eosinophilia in the zona fasciculata of the adrenal gland of one female.	1296724
90-day dietary	Rat	**NOAEL:** 6.3/7.7 mg/kg bw/day in M/F. **LOAEL:** 31.7/36.6 mg/kg bw/day in M/F; decreased cholesterol and triglycerides, increased ALK (F), increased TSH and TBC (F), increased relative kidney weight (M), mineralization of Henle's loops of the kidney (F), enterocyte vacuolation in the jejunum (F), thyroid colloidal alteration (M), thyroid follicular cell hypertrophy (F).	1296608
90-day dietary (low doses)	Dog	**NOAEL:** 9.2/9.3 mg/kg bw/day in M/F. **LOAEL:** 70.9/71.4 mg/kg bw/day in M/F; increased absolute and relative liver weight, increased ALK, decreased T4, increased liver tissue enzymes (N-DEM, O-DEM, P450, ECOD, EH, ALD, GLU-T), decreased GST (M), increased liver triglycerides, cytoplasmic change in the liver.	1296536
90-day dietary (high doses)	Dog	**NOAEL:** Not established as effects were noted at the lowest dose tested. **LOAEL:** 98.4/102.8 mg/kg bw/day in M/F; increased liver tissue enzymes (N-DEM, O-DEM, P450), increased ALK, decreased T4, cortical vacuolation of the adrenal gland, increased liver weight, diffuse hypertrophy of the liver, cytoplasmic change in the liver, fatty change in the liver, increased thymus weight.	1296569
53-week dietary	Dog	**NOAEL:** 11.5/10.8 mg/kg bw/day in M/F. **LOAEL:** 109/117 mg/kg bw/day in M/F; increased serum enzymes (ALK, GLDH), decreased T4, increased liver tissue enzymes (N-DEM, O-DEM, P450), increased liver weight, cytoplasmic change in the liver, inclusions and vacuoles (hyaline bodies) in the liver, decreased adrenal gland weight, small cell type the zona fasciculata of the adrenal gland.	1296570

Study Type	Species	Results[a] (mg/kg/day)	Reference
1-year dietary	Rat	**NOAEL (M):** 6.5 mg/kg bw/day. **NOAEL (F):** 19.3 mg/kg bw/day. **LOAEL (M):** 15.9 mg/kg bw/day; increased T3, thyroid follicular cell hypertrophy, colloidal alteration of the thyroid gland. **LOAEL (F):** 21.7 mg/kg bw/day; decreased body weight and body weight gain, increased P450, increased TSH, decreased bilirubin and cholesterol, thyroid follicular cell hypertrophy, colloidal alteration of the thyroid gland, thyroid follicular cell ectasia, increased uterine weight, dilation and inflammation of the uterus, fluid in the uterus, increased severity of uterine findings (focal glandular hyperplasia, endometrial stromal hyperplasia, hypertrophic luminal epithelium), discoloured adrenal gland, cytoplasmic eosinophilia in the zona fasciculata of the adrenal gland.	1296713
Carcinogenicity (2-year dietary)	Rat	**NOAEL (M):** 6.1 mg/kg bw/day. **NOAEL (F):** 19.5 mg/kg bw/day. **LOAEL (M):** 14.8 mg/kg bw/day; osseous metaplasia of the lung. **LOAEL (F):** 53.5 mg/kg bw/day; decreased body weight and body weight gain, increased girth, vaginal bleeding, pallor, increased TSH, decreased T3 and T4, decreased triglycerides and cholesterol, decreased bilirubin, dilation of the uterus, uterine nodules, change in contents in the uterus, endometritis and metritis, endometrial hyperplasia of the cervix uteri, liver necrosis, colloidal alteration in the thyroid gland, dilation of Rathke's cleft in the pituitary gland.	1296713
Carcinogenicity (18-month dietary)	Mouse	**NOAEL:** 3.3/3.8 mg/kg bw/day in M/F. **LOAEL:** 22/30 mg/kg bw/day in M/F; enlarged adrenal gland (M), cytoplasmic eosinophilia in the zona fasciculata of the adrenal gland, decreased subcapsular hyperplasia (Type A) in the adrenal cortex (F), decreased ceroid deposits in the adrenal cortex (M), decreased diffuse fatty change in the adrenal gland (F), increased severity of amyloidosis (liver, adrenal cortex, thyroid gland), increased incidence of amyloidosis of the pancreas (M), adrenal cortex (F) and stomach (F).	1296588

Study Type	Species	Results[a] (mg/kg/day)	Reference
Two-generation reproduction Study deemed invalid due to low lactation indices in F_2 pups.	Rat	**Parental systemic NOAEL:** 10.2/14.7 mg/kg bw/day in M/F. **Parental systemic LOAEL:** 46/56 mg/kg bw/day in M/F; decreased body weight and body weight loss during lactation (F); decreased body weight during premating (F_1 generation only), decreased body weight during gestation (F_1 generation only), decreased vacuolation in the zona glomerulosa of the adrenal gland (F), thyroid follicular cell hypertrophy, colloidal alteration in the thyroid gland, increased periportal fat content in the liver (F; P generation only). **Offspring systemic NOAEL:** 10.2/14.7 mg/kg bw/day in M/F. **Offspring systemic LOAEL:** 46/56 mg/kg bw/day in M/F; decreased body weight and body weight gain during lactation, decreased spleen and thymus weight. **Reproductive NOAEL:** 46/56 mg/kg bw/day in M/F. **Reproductive LOAEL:** Not established as no reproductive effects were noted.	1296666
Two-generation reproduction Replacement study.	Rat	**Parental systemic NOAEL:** 3.3/3.8 mg/kg bw/day in M/F. **Parental systemic LOAEL:** 13.2/14.2 mg/kg bw/day in M/F; decreased spleen weight (P generation F and F_1 generation M), decreased body weight during pre-mating (F_1 generation only). **Offspring systemic NOAEL:** 2.2/3.8 mg/kg bw/day in M/F. **Offspring systemic LOAEL:** 8.8/14.2 mg/kg bw/day in M/F; decreased body weight during lactation, decreased absolute spleen and thymus weight (M; F_1 generation only). **Reproductive NOAEL:** 13.2/18.0 mg/kg bw/day in M/F. **Reproductive LOAEL:** 76/91 mg/kg bw/day in M/F; increased primordial and decreased growing follicles in the ovary (F_1), delay in sexual maturation (F_1).	1296665

Study Type	Species	Results[a] (mg/kg/day)	Reference
Developmental toxicity	Rat	**Maternal NOAEL:** 10 mg/kg bw/day. **Maternal LOAEL:** 70 mg/kg bw/day; decreased body weight and food consumption. **Developmental NOAEL:** 10 mg/kg bw/day. **Developmental LOAEL:** 70 mg/kg bw/day; "more progressed" ossification of proximal and distal phalangeal bones (i.e. decreased incidence of incompletely ossified phalanges), "more progressed" ossification of skull bones (i.e. decreased incidence of incompletely ossified parietal and intraparietal bones, decreased incidence of enlarged fontanelle, decreased incidence of unossified hyoid bone), increased incidence of incomplete ossification of several cervical vertebral bodies.	1296711
Developmental toxicity	Rabbit	**Maternal NOAEL:** 5 mg/kg bw/day. **Maternal LOAEL:** 35 mg/kg bw/day; increased body weight loss, decreased body weight gain corrected for gravid uterine weight, decreased food consumption, reduced fecal output. **Developmental NOAEL:** 35 mg/kg bw/day. **Developmental LOAEL:** 250 mg/kg bw/day; abortions, increased late resorptions, increased postimplantation loss, two litters with total resorptions, decreased incidence of unossified 5th sternebra, decreased presence of 15th caudal vertebral body, decreased incidence of incompletely ossified hyoid bone.	1296678
Acute Neurotoxicity	Rat	**Systemic NOAEL:** 700 mg/kg bw/day. **Systemic LOAEL:** 2000 mg/kg bw/day; urine staining, decreased motor and locomotor activity. **Neurotoxicity NOAEL:** 2000 mg/kg bw/day. **Neurotoxicity LOAEL:** Not established as effects noted were attributed to systemic toxicity at a high dose.	1296660
Subchronic Neurotoxicity	Rat	**Systemic NOAEL:** 31.8/38.3 mg/kg bw/day. **Systemic LOAEL:** 123/149 mg/kg bw/day; decreased body weight, decreased body weight gain (F), decreased food consumption. **Neurotoxicity NOAEL:** 31.8/38.3 mg/kg bw/day. **Neurotoxicity LOAEL:** 123/149 mg/kg bw/day; clinical signs (aggressive to handler) and FOB[b] findings (rigid upon handling, more energetic reaction to auditory startle and tail pinch) in one F, decreased landing foot splay.	1296661

Study Type	Species	Results[a] (mg/kg/day)	Reference
Immunotoxicity Plaque forming cell assay.	Rat	A NOAEL and LOAEL were not established as this study was considered supplemental. Effects noted at 45.7 mg/kg bw/day in F included discoloured feces and decreased cell count in the spleen. Effects noted at 292/289 mg/kg bw/day in M/F included two deaths (F), increased motility (F), aggression (F), discoloured feces, piloerection, spasms (F), decreased body weight and body weight gain, increased food consumption and decreased cell count in the spleen. There was no effect on the number of IgM antibody plaque forming cells/spleen cell count up to 292/289 mg/kg bw/day in M/F, the highest doses tested. Results from this study indicate that there is no suppression of the humoral immune response.	1296852
Immunotoxicity Plaque forming cell assay.	Mouse	A NOAEL and LOAEL were not established as this study was considered supplemental. Effects noted in M at 163 mg/kg bw/day included decreased cell count in the spleen. Effects noted at 1227/1510 mg/kg bw/day in M/F included decreased body weight and body weight gain (M), decreased water consumption (F), decreased spleen weight and decreased cell count in the spleen (M). There was a slight increase in the number of IgM antibody plaque forming cells/spleen cell count in M at 163 mg/kg bw/day and in F at 1510 mg/kg bw/day. Results from this study indicate that there is no suppression of the humoral immune response up to 1227/1510 mg/kg/day in M/F, the highest doses tested..	1296583
Reverse gene mutation assay	*Salmonella typhimurium/ E.coli*	Negative	1296733
In vitro mammalian chromosomal aberration	Chinese hamster V79 cells	Negative	1296603
In vitro forward gene mutation	Chinese hamster ovary cells	Negative	1296734
In vivo mammalian cytogenetics - micronucleus assay	Mouse	Negative	1296604

Study Type	Species	Results[a] (mg/kg/day)	Reference
Metabolism	Rat	**Absorption** Approximately 48% was absorbed from the gastrointestinal tract after a single low dose (2 mg/kg bw). Absorption following repeated low doses was similar, but was only approximately 9% following a single high dose (500 mg/kg bw). Absorption was rapid after a single low dose (peak plasma concentration at 1–2 hours) but was slower after repeated low doses and after a single high dose (peak plasma concentrations of 3–4 and 6 hours, respectively). **Distribution** Very little radioactivity remained in the tissues and carcass at 72 hours post-dose (<0.6%) regardless of dosing regimen. Concentrations of radioactivity in tissues were slightly higher following repeat dosing compared to single dosing, and were lower following administration of the high dose when compared to the low dose. The highest levels of radioactivity were detected in the carcass for all dosing regimens. Tissues with detectable levels of radioactivity were the liver, gastrointestinal tract, fat, skin (low dose only), blood, kidney and ovaries. **Excretion** The majority of Spiromesifen is eliminated within 24 hours. Fecal excretion was the major route of elimination (53–57% following single and repeated low doses, 90% following a single high dose) followed by urinary excretion (34–40% following single and repeated low doses, 9% following a single high dose). Biliary excretion was minor (7%) following a single low dose. Excretion via expired air is negligible (<0.01%) and urinary excretion comprises 8–29% of total. Within 48 hours, virtually all of administered Spiromesifen was excreted. **Metabolism** Orally administered Spiromesifen is extensively metabolized. The primary urinary metabolites were BSN 2060-4-hydroxymethyl (8.9-10.8% in males and 5.5–6.5% in females) and BSN 2060-enol (2.5–4.2% in males and 8.1–9.1% in females). The parent compound was largely unmetabolized in the feces (33.5–40.7% at the low dose and 83.7% at the high dose). The only metabolite identified in the feces of both males and females was BSN 2060-enol (1.8–2.8%).	1296663

[a] Effects observed in males (M) as well as females (F) unless otherwise reported
[b] Functional observational battery

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

Exposure Scenario	Dose (mg/kg bw/day)	Study	Endpoint	MOE	Reference
Acute dietary	Not required as no endpoint of concern attributable to a single dose was identified.				
Chronic dietary, all populations	NOAEL = 2.2	2-generation reproductive toxicity study in rats	Decreased spleen weight in parental females and decreased body and organ (spleen and thymus) weights in offspring.	N/A	1296665
	ADI = 0.007 mg/kg bw/day (based on the NOAEL of 2.2 mg/kg bw/day and an UF of 300)				
Short-, intermediate- and long-term dermal and inhalation	NOAEL = 2.2	2-generation reproductive toxicity study in rats	Decreased spleen weight in parental females and decreased body and organ (spleen and thymus) weights in offspring.	300	1296665

Table 5 Integrated Food Residue Chemistry Summary

NATURE OF THE RESIDUE IN PLANTS – LETTUCE		**PMRA # 1296573**
Radiolabel Position	**3-Dihydrofuranone**	
Test site	Plastic-covered polytunnel protected from normal climatic conditions.	
Treatment	The formulation was applied foliarly to the lettuce plants through slits in the polyethylene using a spray gun.	
Rate	340 g a.i./ha (first application) 308 g a.i./ha (second application)	
End-use product	Spiromesifen, formulated as a 240 g a.i./L SC (soluble concentrate)	
Preharvest interval	7 days	
The total radioactive residues (TRRs) in lettuce (leaves) were 0.411 ppm.		
Metabolites Identified **Matrix**	**Major Metabolites (>10% TRRs)**	**Minor Metabolites (<10% TRRs)**
lettuce leaves	Spiromesifen (BSN 2060), BSN 2060-4-hydroxymethyl-glucoside	BSN 2060-enol, cis- or trans-BSN 2060-3-pentanol, BSN 2060-4-hydroxymethyl, BSN 2060-dihydroxy-enol

NATURE OF THE RESIDUE IN PLANTS –COTTON		PMRA #1296581
Radiolabel Position	**3-Dihydrofuranone**	
Test site	Four one-gallon pots maintained in an enclosed greenhouse.	
Treatment	Foliar broadcast treatment by CO_2-powered small-plot sprayer. Areas completely enclosed with plastic (spray booths); applications made approximately 25 feet from the greenhouse storage area	
Rate	281 g a.i./ha (first application) 281 g a.i./ha (second application) 347 g a.i./ha (third application) 826 g a.i./ha (first application) 825 g a.i./ha (second application) 905 g a.i./ha (third application)	
End-use product	Spiromesifen, formulated as a 240 g a.i./L SC (soluble concentrate)	
Preharvest interval	21 days	
The majority of the total radioactive residues (TRRs) were in gin by-products (6.33 ppm), compared to undelinted treated seed (0.051 ppm). From the undelinted seed, the majority of the TRRs were in the seed lint (0.039 ppm), compared to the delinted seed (0.012 ppm).		
Metabolites Identified **Matrix**	**Major Metabolites (>10% TRRs)**	**Minor Metabolites (<10% TRRs)**
Seed lint	Spiromesifen (BSN 2060), BSN 2060-enol	None
Delinted seed	Spiromesifen (BSN 2060)	BSN 2060-enol
Gin-byproducts	Spiromesifen (BSN 2060), BSN 2060-enol	cis- or trans-BSN 2060-3-pentanol, BSN 2060-4-hydroxymethyl, BSN 2060-dihydroxy-enol, cis- or trans-BSN 2060-4-hydroxymethyl-3-pentanol, BSN 2060-4-hydroxymethyl-glucoside
NATURE OF THE RESIDUE IN PLANTS – TOMATOES		**PMRA #1296580**
Radiolabel Position	**3-Dihydrofuranone**	
Test site	Plastic-covered polytunnel protected from normal climatic conditions	
Treatment	The formulation was applied foliarly (broadcast) to the tomato plants through slits in the polyethylene using a spray gun for 1X treatment. The 3X treatment was applied foliarly by paintbrush to tomato fruit.	

Radiolabel Position	3-Dihydrofuranone
Rate	1X 439 g a.i./ha (first application) 378 g a.i./ha (second application) 3X 2.45 kg a.i./ha (only one application)
End-use product	Spiromesifen, formulated as a 240 g a.i./L SC (soluble concentrate)
Preharvest interval	7 days

The majority of the total radioactive residues (TRRs) were in ripe fruit (0.844 ppm), compared to nonripe fruit (0.496 ppm). Surface residues in both ripe and nonripe fruit contained the most TRRs at 0.669 ppm and 0.365 ppm (73.5-79.3% of the TRRs) respectively; rather than in extracts (0.143 ppm and 0.123 ppm, respectively) or residues (0.032 ppm and 0.009 ppm, respectively).

Metabolites Identified Matrix	Major Metabolites (>10% TRRs)	Minor Metabolites (<10% TRRs)
Ripe Fruit	Spiromesifen (BSN 2060)	BSN 2060-enol, BSN 2060-4-hydroxymethyl, BSN 2060-4-hydroxymethyl-glucoside
Nonripe fruit	Spiromesifen (BSN 2060)	BSN 2060-enol, BSN 2060-4-hydroxymethyl, BSN 2060-4-hydroxymethyl-glucoside

Based on the predominant residues and toxicological significance, the residue definition is Spiromesifen (BSN 2060) and BSN 2060-enol for enforcement purposes in primary crops. For risk assessment purposes, the residue definition is spiromesifen, BSN 2060-enol and BSN 2060-4-hydroxymethyl (free and conjugated).

CONFINED ROTATIONAL CROP STUDY USING RADISH, MUSTARD, WHEAT, SORGHUM		PMRA #1296274
Radiolabel Position	**3-Dihydrofuranone**	
Test site	Plastic containers (50 × 70 × 30 cm deep) filled with sandy loam soil. Kept in an environmentally controlled growth chamber.	
Formulation used for trial	Spiromesifen, formulated as a 240 g a.i./L SC (soluble concentrate)	
Application rate and timing	1 application at 803–804 g a.i./ha 30 days before the first sowing of rotational crops	
Matrix	**Plantback Interval**	**Overall TRRs (ppm)**
Soil in wheat pot	Postapplication Aged for 30 days Aged for 187 days Aged for 365 days	0.407 0.643 0.377 0.187
Soil in spinach pot	Postapplication Aged for 30 days Aged for 130 days Aged for 365 days	0.633 0.276 0.295 0.158

Matrix	Plantback Interval	Overall TRRs (ppm)
Soil in turnip pot	Postapplication Aged for 30 days Aged for 120 days Aged for 365 days	0.546 0.281 0.310 0.212
Wheat forage	Soil aged for 30 days Soil aged for 187 days Soil aged for 365 days	0.640 0.062 0.033
Wheat hay	Soil aged for 30 days Soil aged for 187 days Soil aged for 365 days	0.542 0.316 0.279
Wheat straw	Soil aged for 30 days Soil aged for 187 days Soil aged for 365 days	1.149 0.520 0.353
Wheat grain	Soil aged for 30 days Soil aged for 187 days Soil aged for 365 days	0.027 0.180 0.082
Spinach	Soil aged for 30 days Soil aged for 130 days Soil aged for 365 days	0.315 0.198 0.043
Turnip foliage	Soil aged for 30 days Soil aged for 120 days Soil aged for 365 days	0.169 0.129 0.025
Turnip root	Soil aged for 30 days Soil aged for 120 days Soil aged for 365 days	0.079 0.034 0.010
Metabolites Identified	**Major Metabolites (> 10% TRRs)**	**Minor Metabolites (< 10% TRRs)**
Matrix	**3-Dihydrofuranone**	**3-Dihydrofuranone**
30 day PBI		
Wheat forage	BSN 2060-4-hydroxymethyl-glucoside, BSN 2060-dihydroxy-enol,	Spiromesifen (BSN 2060) , BSN 2060-enol, BSN 2060-4-hydroxymethyl, cis- or trans-BSN 2060-3-pentanol, BSN 2060-2-hydroxymethyl, conjugate of BSN 2060-4-hydroxymethyl

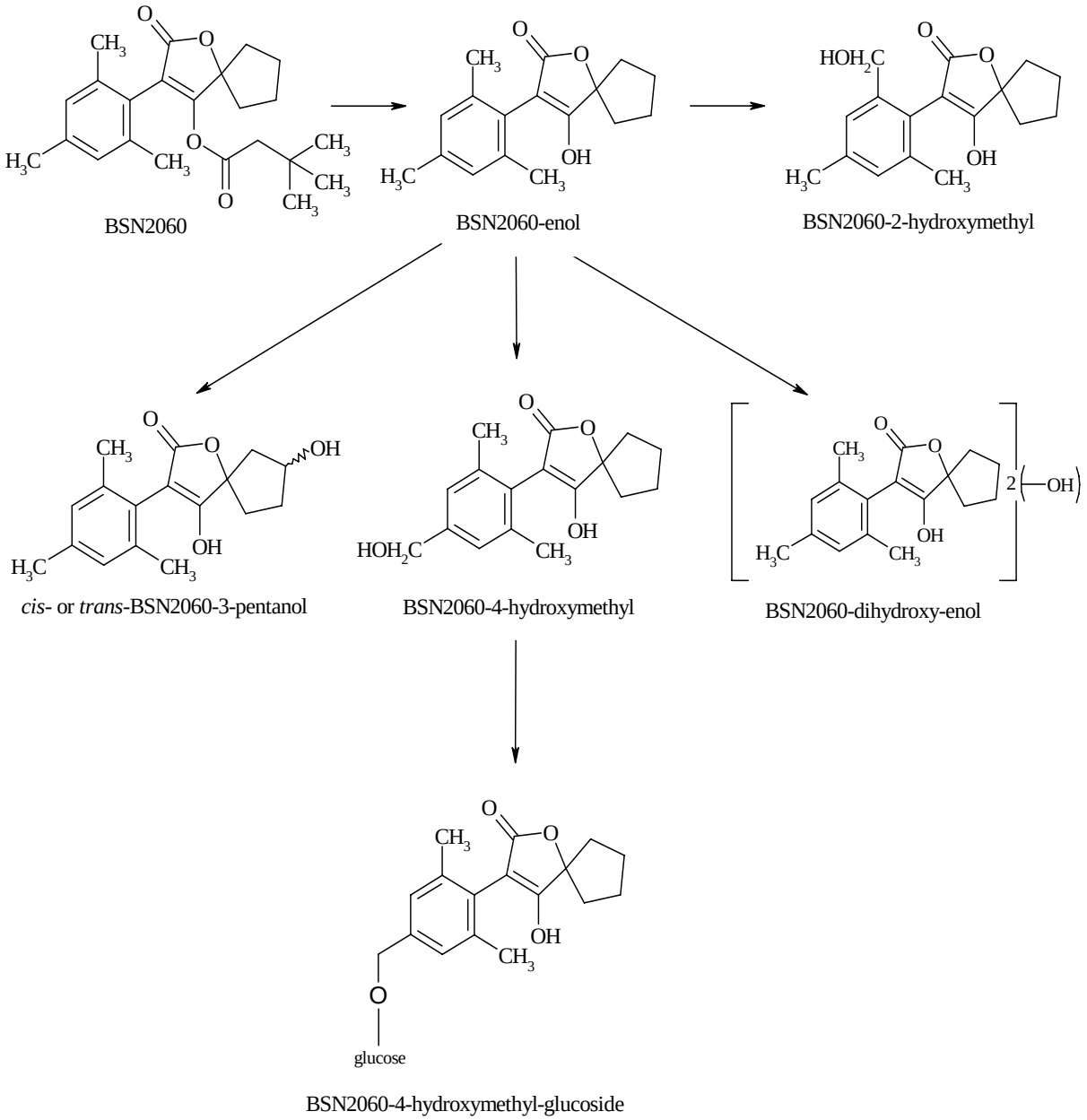
Matrix	Plantback Interval	Overall TRRs (ppm)
Wheat hay	BSN 2060-4-hydroxymethyl-glucoside, conjugate of BSN 2060-4-hydroxymethyl	Spiromesifen (BSN 2060) , BSN 2060-enol, BSN 2060-4-hydroxymethyl, cis- or trans-BSN 2060-3-pentanol, BSN 2060-dihydroxy-enol, BSN 2060-2-hydroxymethyl
Wheat straw	BSN 2060-4-hydroxymethyl-glucoside, conjugate of BSN 2060-4-hydroxymethyl	Spiromesifen (BSN 2060) , BSN 2060-enol, BSN 2060-4-hydroxymethyl, cis- or trans-BSN 2060-3-pentanol, BSN 2060-dihydroxy-enol, BSN 2060-2-hydroxymethyl
Wheat grain	BSN 2060-4-hydroxymethyl-glucoside, BSN 2060-dihydroxy-enol	Spiromesifen (BSN 2060) , BSN 2060-enol, BSN 2060-4-hydroxymethyl, cis- or trans-BSN 2060-3-pentanol, BSN 2060-2-hydroxymethyl, conjugate of BSN 2060-4-hydroxymethyl
Spinach	BSN 2060-4-hydroxymethyl-glucoside	Spiromesifen (BSN 2060) , BSN 2060-enol, BSN 2060-4-hydroxymethyl, cis- or trans-BSN 2060-3-pentanol, BSN 2060-dihydroxy-enol, BSN 2060-2-hydroxymethyl, conjugate of BSN 2060-4-hydroxymethyl
Turnip Foliage	BSN 2060-4-hydroxymethyl, BSN 2060-4-hydroxymethyl-glucoside, cis- or trans-BSN 2060-3-pentanol	Spiromesifen (BSN 2060) , BSN 2060-enol, BSN 2060-dihydroxy-enol, BSN 2060-2-hydroxymethyl, conjugate of BSN 2060-4-hydroxymethyl
Turnip Root	BSN 2060-enol, BSN 2060-4-hydroxymethyl, cis- or trans-BSN 2060-3-pentanol	Spiromesifen (BSN 2060) , BSN 2060-4-hydroxymethyl-glucoside, BSN 2060-dihydroxy-enol, BSN 2060-2-hydroxymethyl, conjugate of BSN 2060-4-hydroxymethyl
120−187 day PBI		
Wheat forage	BSN 2060-4-hydroxymethyl-glucoside, BSN 2060-dihydroxy-enol,	Spiromesifen (BSN 2060) , BSN 2060-enol, BSN 2060-4-hydroxymethyl, cis- or trans-BSN 2060-3-pentanol, BSN 2060-2-hydroxymethyl, conjugate of BSN 2060-4-hydroxymethyl
Wheat hay	BSN 2060-4-hydroxymethyl-glucoside	Spiromesifen (BSN 2060) , BSN 2060-enol, BSN 2060-4-hydroxymethyl, cis- or trans-BSN 2060-3-pentanol, BSN 2060-dihydroxy-enol, BSN 2060-2-hydroxymethyl, conjugate of BSN 2060-4-hydroxymethyl

Matrix	Plantback Interval	Overall TRRs (ppm)
Wheat straw	BSN 2060-4-hydroxymethyl-glucoside	Spiromesifen (BSN 2060) , BSN 2060-enol, BSN 2060-4-hydroxymethyl, cis- or trans-BSN 2060-3-pentanol, BSN 2060-dihydroxy-enol, BSN 2060-2-hydroxymethyl, conjugate of BSN 2060-4-hydroxymethyl
Wheat grain	None	Spiromesifen (BSN 2060) , BSN 2060-enol, BSN 2060-4-hydroxymethyl, BSN 2060-4-hydroxymethyl-glucoside, cis- or trans-BSN 2060-3-pentanol, BSN 2060-dihydroxy-enol, BSN 2060-2-hydroxymethyl, conjugate of BSN 2060-4-hydroxymethyl
Spinach	BSN 2060-4-hydroxymethyl-glucoside, cis- or trans-BSN 2060-3-pentanol, BSN 2060-dihydroxy-enol	Spiromesifen (BSN 2060) , BSN 2060-enol, BSN 2060-4-hydroxymethyl, BSN 2060-2-hydroxymethyl, conjugate of BSN 2060-4-hydroxymethyl
Turnip Foliage	BSN 2060-4-hydroxymethyl-glucoside, cis- or trans-BSN 2060-3-pentanol, BSN 2060-4-hydroxymethyl	Spiromesifen (BSN 2060) , BSN 2060-enol, BSN 2060-2-hydroxymethyl, BSN 2060-dihydroxy-enol, conjugate of BSN 2060-4-hydroxymethyl
Turnip Root	BSN 2060-4-hydroxymethyl	Spiromesifen (BSN 2060) , BSN 2060-enol, BSN 2060-4-hydroxymethyl-glucoside, cis- or trans-BSN 2060-3-pentanol, BSN 2060-dihydroxy-enol, BSN 2060-2-hydroxymethyl, conjugate of BSN 2060-4-hydroxymethyl
365 d PHI		
Wheat forage	BSN 2060-4-hydroxymethyl-glucoside	Spiromesifen (BSN 2060) , BSN 2060-enol, BSN 2060-4-hydroxymethyl, cis- or trans-BSN 2060-3-pentanol, BSN 2060-dihydroxy-enol, BSN 2060-2-hydroxymethyl, conjugate of BSN 2060-4-hydroxymethyl
Wheat hay	BSN 2060-4-hydroxymethyl-glucoside, BSN 2060-dihydroxy-enol,	Spiromesifen (BSN 2060) , BSN 2060-enol, BSN 2060-4-hydroxymethyl, cis- or trans-BSN 2060-3-pentanol, BSN 2060-2-hydroxymethyl, conjugate of BSN 2060-4-hydroxymethyl
Wheat straw	BSN 2060-4-hydroxymethyl-glucoside, cis- or trans-BSN 2060-3-pentanol, BSN 2060-dihydroxy-enol,	Spiromesifen (BSN 2060) , BSN 2060-enol, BSN 2060-4-hydroxymethyl, BSN 2060-2-hydroxymethyl, conjugate of BSN 2060-4-hydroxymethyl

Matrix	Plantback Interval	Overall TRRs (ppm)
Wheat grain	None	Spiromesifen (BSN 2060) , BSN 2060-enol, BSN 2060-4-hydroxymethyl, BSN 2060-4-hydroxymethyl-glucoside, cis- or trans-BSN 2060-3-pentanol, BSN 2060-dihydroxy-enol, BSN 2060-2-hydroxymethyl, conjugate of BSN 2060-4-hydroxymethyl
Spinach	cis- or trans-BSN 2060-3-pentanol	Spiromesifen (BSN 2060) , BSN 2060-enol, BSN 2060-4-hydroxymethyl, BSN 2060-4-hydroxymethyl-glucoside, BSN 2060-dihydroxy-enol, BSN 2060-2-hydroxymethyl, conjugate of BSN 2060-4-hydroxymethyl
Turnip Foliage	None	Spiromesifen (BSN 2060) , BSN 2060-enol, BSN 2060-4-hydroxymethyl, BSN 2060-4-hydroxymethyl-glucoside, cis- or trans-BSN 2060-3-pentanol, BSN 2060-dihydroxy-enol, BSN 2060-2-hydroxymethyl, conjugate of BSN 2060-4-hydroxymethyl
Turnip Root	Not performed	Not performed
Based on the predominant residues and toxicological significance, the residue definition is Spiromesifen (BSN 2060), BSN 2060-enol and BSN 2060-4-hydroxymethyl (free and conjugated) for enforcement purposes in rotational crops. For risk assessment purposes, the residue definition is spiromesifen, BSN 2060-enol and BSN 2060-4-hydroxymethyl (free and conjugated).		

Matrix	Plantback Interval	Overall TRRs (ppm)

Proposed Metabolic Profile in Rotational Wheat, Turnip and Spinach



NATURE OF THE RESIDUE IN LAYING HEN	PMRA #1296692

Seven Lohmann Brown laying hens were dosed for 3 consecutive days with spiromesifen (radiolabelled in the 3-dihydrofuranone position) at 10 mg/kg bw/day (190 ppm in the diet). Hens were sacrificed approximately 5 hours after the final dose was administered.

Matrices	% of the Administered Dose
Excreta	78.9 (0–24 hours) 78.6 (24–48 hours) 58.3 (48–53 hours)
Cage wash	2.8 (0–24 hours) 3.2 (24–48 hours) 4.2 (48–53 hours)
Liver	0.1 (1.68 ppm)
Muscle	0.1 (0.067 ppm)
Fat	<0.1 (0.050 ppm)
Skin	<0.1 (0.380 ppm)
Eggs	<0.1 (<0.005 ppm) –24 to 0 hours <0.1 (<0.006 ppm) 0–24 hours <0.1 (0.020 ppm) 24–48 hours <0.1 (0.032 ppm) 48–53 hours
Total	62.7%

Metabolites Identified	Major Metabolites (>10% TRRs)	Minor Metabolites (<10% TRRs)
Radiolabel Position	**3-Dihydrofuranone**	**3-Dihydrofuranone**
Excreta	BSN 2060 (spiromesifen)	BSN 2060-enol, BSN 2060-enol-glucuronide, BSN 2060-2-hydroxymethyl, BSN 2060-3-pentanol, BSN 2060-4-hydroxymethyl, BSN 2060-4-or-2-hydroxymethyl-3-pentanol, BSN 2060-4-carboxy-3-pentanol, BSN 2060-hydroxy-4-carboxy, BSN 2060-dihydroxy-4-carboxy
Liver	BSN 2060-enol, BSN 2060-4-hydroxymethyl, BSN 2060-4-carboxy-3-pentanol, BSN 2060-hydroxy-4-carboxy,	BSN 2060 (spiromesifen) BSN 2060-enol-glucuronide, BSN 2060-2-hydroxymethyl, BSN 2060-3-pentanol, BSN 2060-4-or-2-hydroxymethyl-3-pentanol, BSN 2060-aldehyde, BSN 2060-dihydroxy-4-carboxy
Muscle	BSN 2060-enol	BSN 2060 (spiromesifen), BSN 2060-enol-glucuronide, BSN 2060-2-hydroxymethyl, BSN 2060-3-pentanol, BSN 2060-4-hydroxymethyl, BSN 2060-4-or-2-hydroxymethyl-3-pentanol, BSN 2060-4-carboxy-3-pentanol, BSN 2060-hydroxy-4-carboxy, BSN 2060-dihydroxy-4-carboxy

Fat	BSN 2060 (spiromesifen)	BSN 2060-enol, BSN 2060-enol-glucuronide, BSN 2060-2-hydroxymethyl, BSN 2060-3-pentanol, BSN 2060-4-hydroxymethyl, BSN 2060-4-or-2-hydroxymethyl-3-pentanol, BSN 2060-4-carboxy-3-pentanol, BSN 2060-hydroxy-4-carboxy, BSN 2060-dihydroxy-4-carboxy
Skin	BSN 2060-enol, BSN 2060-4-carboxy-3-pentanol, BSN 2060-hydroxy-4-carboxy,	BSN 2060 (spiromesifen), BSN 2060-enol-glucuronide, BSN 2060-2-hydroxymethyl, BSN 2060-3-pentanol, BSN 2060-4-hydroxymethyl, BSN 2060-4-or-2-hydroxymethyl-3-pentanol, BSN 2060-dihydroxy-4-carboxy
Eggs	BSN 2060 (spiromesifen), BSN 2060-enol,	BSN 2060-enol-glucuronide, BSN 2060-2-hydroxymethyl, BSN 2060-3-pentanol, BSN 2060-4-hydroxymethyl, BSN 2060-4-or-2-hydroxymethyl-3-pentanol, BSN 2060-4-carboxy-3-pentanol, BSN 2060-hydroxy-4-carboxy, BSN 2060-dihydroxy-4-carboxy

Based on the predominant residues and toxicological significance, the residue definition is Spiromesifen (BSN 2060) and BSN 2060-enol for enforcement purposes. For risk assessment purposes the residue definition is spiromesifen, BSN 2060-enol, BSN 2060-4-carboxy-3-pentanol and BSN 2060-hydroxy-4-carboxy.

NATURE OF THE RESIDUE IN LACTATING GOAT	**PMRA #1296668**

One lactating goat (British Saanen) was dosed for 3 consecutive days with spiromesifen (radiolabelled in the 3-dihydrofuranone position) at 10 mg/kg bw/day (344 ppm in the diet). The goat was sacrificed 6 hours after the final dose was administered.

Matrices	**% of Administered Dose**
Urine	12.4 (0–24 hours) 16.8 (24–48 hours) 3.87 (48–54 hours)
Cage Wash	1.04 (0–54 hours)
Feces	1.67 (0–24 hours) 9.73 (24–48 hours) 3.55 (48–54 hours)
Muscle	0.23 (0.33 ppm)
Fat	0.20 (0.50 ppm)
Kidney	0.10 (8.41 ppm)
Liver	0.31 (3.82 ppm)

Milk	<0.01 (0.08 ppm) Day 1 pooled sample <0.01 (0.11 ppm) Day 2 pooled sample <0.01 (0.16 ppm) Day 3 a.m. sample
Blood	(0.81 ppm)
Bile	(78.9 ppm)

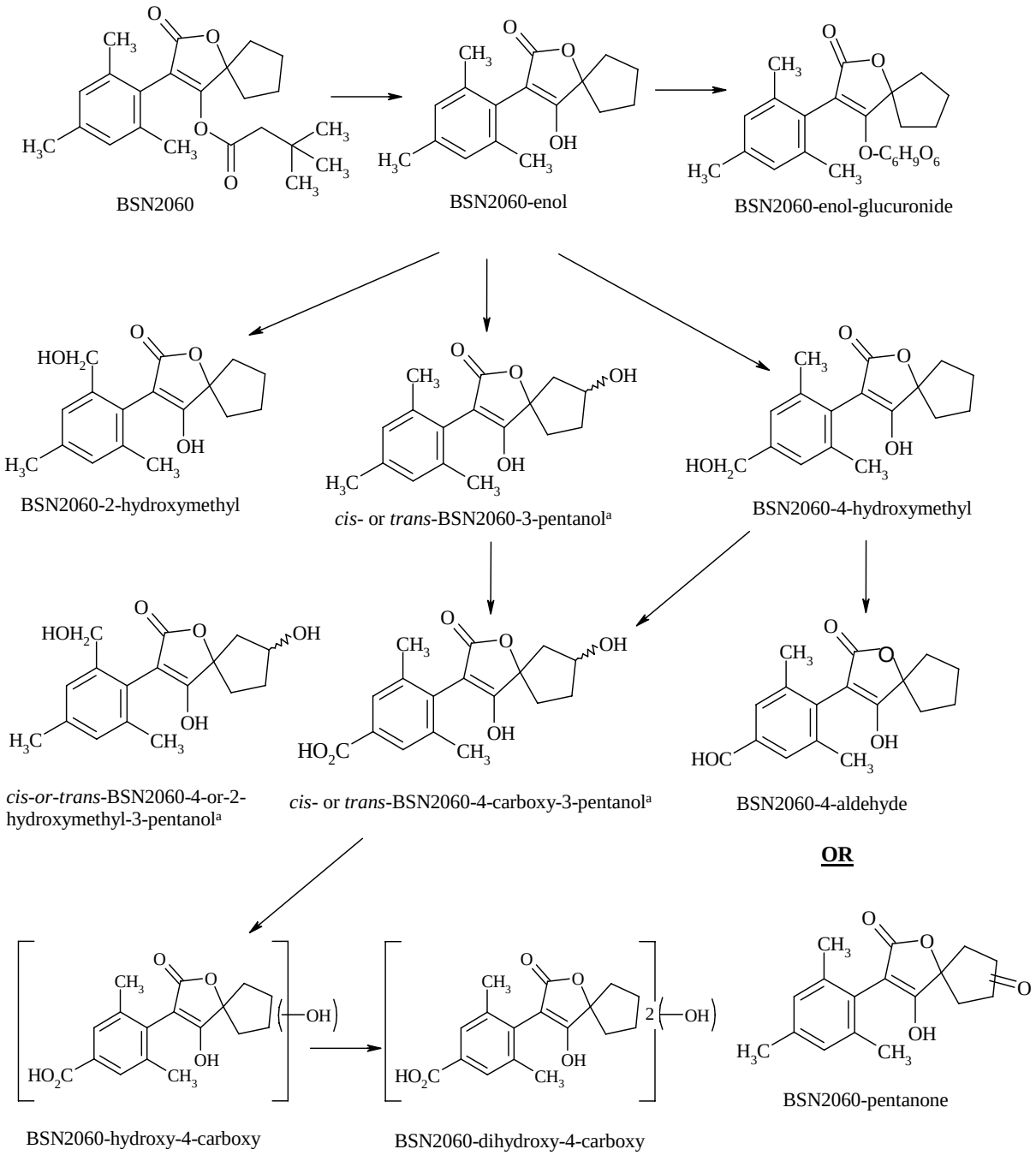
Metabolites Identified	**Major Metabolites (>10% TRRs)**	**Minor Metabolites (<10% TRRs)**
Radiolabel Position	**3-Dihydrofuranone**	**3-Dihydrofuranone**
Urine	BSN 2060-enol	BSN 2060 (spiromesifen)
Liver	BSN 2060-enol, BSN 2060-enol-glucuronide	BSN 2060 (spiromesifen), BSN 2060-2-hydroxymethyl and 4-carboxylic acid, BSN 2060-3 or 4-pentanol isomers, BSN 2060-4-hydroxymethyl, BSN 2060-4-hydroxymethyl-glucuronide, BSN 2060-hydroxy-3-pentanol or BSN 2060-4-carboxy-3-pentanol
Kidney	BSN 2060-enol	BSN 2060 (spiromesifen), BSN 2060-enol-glucuronide, BSN 2060-2-hydroxymethyl and 4-carboxylic acid, BSN 2060-3 or 4-pentanol isomers, BSN 2060-4-hydroxymethyl, BSN 2060-4-hydroxymethyl-glucuronide
Fat	BSN 2060 (spiromesifen), BSN 2060-enol	None
Muscle	BSN 2060-enol	BSN 2060 (spiromesifen), BSN 2060-2-hydroxymethyl and 4-carboxylic acid, BSN 2060-3 or 4-pentanol isomers, BSN 2060-4-hydroxymethyl
Milk	BSN 2060 (spiromesifen), BSN 2060-enol, BSN 2060-4-hydroxymethyl	BSN 2060-2-hydroxymethyl and 4-carboxylic acid

Based on the predominant residues and toxicological significance, the residue definition is Spiromesifen (BSN 2060), BSN 2060-enol (free and conjugated) and BSN 2060-4-hydroxymethyl (free and conjugated) for enforcement purposes. For risk assessment purposes, the residue definition is spiromesifen, BSN 2060-enol (free and conjugated) and BSN 2060-4-hydroxymethyl (free and conjugated).

OVERALL CONCLUSION

Spiromesifen is metabolized in all RACs by the loss of the dimethylbutyric acid group to yield BSN 2060-enol. Further metabolism can include hydroxylation of BSN 2060-enol to yield BSN 2060-2-hydroxymethyl or BSN 2060-4-hydroxymethyl; hydroxylation of BSN 2060-enol to yield BSN 2060-3-pentanol; oxidation of BSN 2060-3-pentanol or BSN 2060-2- or -4-hydroxymethyl to give BSN 2060-2- or -4-hydroxymethyl-3-pentanol; oxidation of BSN 2060-4-hydroxymethyl to give BSN 2060-pentanone or BSN 2060-4-aldehyde; oxidation of BSN 2060-2- or 4-hydroxymethyl-3-pentanol to give BSN 2060-hydroxy-4-carboxy; and further hydroxylation of BSN 2060-4-hydroxymethyl-3-pentanol or BSN 2060-hydroxy-4-carboxy to give BSN 2060-dihydroxy-4-carboxy. The reviewed plant studies also indicate spiromesifen, when foliarly applied during the vegetative growth stage, is not readily translocated.

Proposed Metabolic Scheme in Plants, Livestock



[a]One possible isomer shown.

CROP FIELD TRIALS ON POTATO									**PMRA # 1296180**
During the 2000 and 2001 potato growing seasons, field trials were conducted at 16 locations to evaluate the magnitude of residue in/on potatoes following the application of end-use product BSN 2060 240 SC. Trial sites were in regions 1 (PA, NY; 2 trials), 2 (GA; 1 trial), 3 (FL; 1 trial), 5 (NE, KS, IN, SD; 4 trials), 9 (UT; 1 trial), 10 (CA; 1 trial) and 11 (ID, WA, OR; 6 trials). Since residue levels for spiromesifen were <LOQ (<0.01 ppm), there was no decline in residues over time.									
Potato trials conducted with the end-use product BSN 2060 240 SC (LOQ = 0.01 ppm)									
Commodity	**Total Applic. Rate kg a.i./ha**	**PHI (days)**	**Residue Levels (ppm)**						
			n	**Min.**	**Max.**	**HAFT**	**Median (STMdR)**	**Mean (STMR)**	**Std. Dev.**
BSN 2060 (parent - Spiromesifen)									
Tuber	0.533–0.578	7	36	<0.01	<0.01	<0.01	0.01	0.01	0
BSN 2060-enol (metabolite)									
Tuber	0.533–0.578	7	36	<0.01	<0.01	<0.01	0.01	0.01	0
Total Spiromesifen Residues									
Tuber	0.533–0.578	7	36	<0.02	<0.02	<0.02	0.02	0.02	0

CROP FIELD TRIALS ON STRAWBERRY									**PMRA # 1296173**
During the 2000 strawberry growing season, field trials were conducted at 8 locations to evaluate the magnitude of residue in/on strawberries following three broadcast foliar applications of end-use product BSN 2060 240 SC. Trial sites were in regions 1 (PA; 1 trial), 2 (NC; 1 trial), 3 (FL; 1 trial), 5 (OH; 1 trial), 10 (CA; 3 trials) and 12 (OR; 1 trial). Residue decline data show that spiromesifen-derived residues decrease in strawberries with increasing PHIs.									
Strawberry trials conducted with the end-use product BSN 2060 240 SC (LOQ = 0.01 ppm)									
Commodity	**Total Applic. Rate kg a.i./ha**	**PHI (days)**	**Residue Levels (ppm)**						
			n	**Min.**	**Max.**	**HAFT**	**Median (STMdR)**	**Mean (STMR)**	**Std. Dev.**
BSN 2060 (parent - Spiromesifen)									
Strawberries	0.863	0	2	1.12	1.42	1.27	1.27	1.27	0.21
	0.843–0.863	2–4	16	0.17	1.52	1.48	0.46	0.65	0.5
		7–9	16	0.13	1.13	0.97	0.31	0.42	0.32
		12–15	16	0.12	0.35	0.33	0.2	0.22	0.07
	0.863	22	2	0.03	0.03	0.03	0.03	0.03	0.01
		28	2	0.07	0.1	0.08	0.08	0.08	0.02

BSN 2060-enol (metabolite)									
Strawberries	0.863	0	2	0.09	0.11	0.1	0.1	0.1	0.02
	0.843–0.863	2–4	16	0.04	0.15	0.14	0.08	0.09	0.03
		7–9	16	0.04	0.16	0.16	0.09	0.1	0.04
		12–15	16	0.04	0.14	0.14	0.1	0.1	0.03
	0.863	22	2	0.07	0.08	0.08	0.08	0.08	0.01
		28	2	0.06	0.06	0.06	0.06	0.06	0
Total Spiromesifen Residues									
Strawberries	0.863	0	2	1.21	1.53	1.37	1.37	1.37	0.23
	0.843–0.863	2–4	16	0.23	1.64	1.57	0.54	0.73	0.52
		7–9	16	0.2	1.28	1.12	0.41	0.51	0.35
		12–15	16	0.18	0.48	0.47	0.31	0.32	0.08
	0.863	22	2	0.11	0.11	0.11	0.11	0.11	0
		28	2	0.13	0.16	0.14	0.14	0.14	0.02

CROP FIELD TRIALS ON MUSTARD GREENS **PMRA # 1296172**

During the 2000 mustard greens growing season, field trials were conducted at 5 locations to evaluate the magnitude of residue in/on mustard greens following three foliar applications of end-use product BSN 2060 240 SC. Trial sites were in regions 2 (GA; 1 trial), 4 (MS; 1 trial), 5 (IN; 1 trial), 6 (TX; 1 trial) and 10 (CA; 1 trial). Residue decline data indicated that spiromesifen-derived residues decreased in mustard greens with increasing PHIs.

Mustard greens trials conducted with the end-use product BSN 2060 240 SC (LOQ = 0.01 ppm)

Commodity	**Total Applic. Rate kg a.i./ha**	**PHI (days)**	**Residue Levels (ppm)**						
			n	**Min.**	**Max.**	**HAFT**	**Median (STMdR)**	**Mean (STMR)**	**Std. Dev.**
BSN 2060 (parent - Spiromesifen)									
Mustard greens	0.453	0	2	3.28	7.75	5.52	5.52	5.52	3.16
	0.448–0.453	6–8	10	0.45	9.58	9.44	1.18	2.83	3.53
		13–14	10	0.05	5.57	5.28	0.44	1.3	2.11
	0.453	21	2	0.16	0.19	0.18	0.18	0.18	0.02
		28	2	0.07	0.08	0.08	0.08	0.08	0.01
BSN 2060-enol (metabolite)									
Mustard greens	0.453	0	2	0.55	0.66	0.6	0.6	0.6	0.08
	0.448–0.453	6–8	10	0.17	0.61	0.53	0.25	0.29	0.14
		13–14	10	0.03	0.22	0.21	0.13	0.12	0.08
	0.453	21	2	0.05	0.06	0.05	0.05	0.05	0
		28	2	0.03	0.03	0.03	0.03	0.03	0

Total Spiromesifen Residues									
Mustard greens	0.453	0	2	3.83	8.41	6.12	6.12	6.12	3.24
	0.448–0.453	6–8	10	0.63	10.03	9.97	1.4	3.13	3.66
		13–14	10	0.08	5.79	5.48	0.57	1.42	2.17
	0.453	21	2	0.21	0.25	0.23	0.23	0.23	0.02
		28	2	0.1	0.11	0.1	0.1	0.1	0

CROP FIELD TRIALS ON FIELD CORN **PMRA # 1296179**

During the 2000 field corn growing season, field trials were conducted at 20 locations to evaluate the magnitude of residue in/on corn forage, corn stover and corn grain following two broadcast foliar applications of end-use product BSN 2060 240 SC. Trial sites were in regions 1 (PA; 1 trial), 2 (GA; 1 trial), 5 (IL, NE, KS, IN, IA, ND; 17 trials) and 6 (OK; 1 trial). Generally, the total residues on corn forage and stover appeared to decline with time.

Field corn trials conducted with the end-use product BSN 2060 240 SC (LOQ = 0.01 ppm)

Commodity	Total Applic. Rate kg a.i./ha	PHI (days)	Residue Levels (ppm)						
			n	Min.	Max.	HAFT	Median (STMdR)	Mean (STMR)	Std. Dev.
BSN 2060 (parent - Spiromesifen)									
Corn forage	0.292–0.308	0–13	20	0.08	2.56	1.905	0.882	0.942	0.565
Corn stover		28–32	20	<0.01	1.75	1.435	0.341	0.376	0.354
Corn grain		28–32	20	<0.01	<0.01	<0.01	0.01	0.01	0
BSN 2060-enol (metabolite)									
Corn forage	0.292–0.308	0–13	20	0.07	1.38	0.994	0.291	0.323	0.264
Corn stover		28–32	20	<0.01	1.15	1.048	0.292	0.389	0.307
Corn grain		28–32	20	<0.01	<0.01	<0.01	0.01	0.01	0
Total Spiromesifen Residues									
Corn forage	0.292–0.308	0–13	20	0.225	2.81	2.265	1.221	1.266	0.616
Corn stover		28–32	20	0.02	2.059	1.825	0.617	0.759	0.5
Corn grain		28–32	20	<0.02	<0.02	<0.02	0.02	0.02	0

CROP FIELD TRIALS ON PEPPER AND TOMATO **PMRA # 1296175**

During the 2000 pepper and tomato growing season, field trials were conducted at 21 locations to evaluate the magnitude of residue in/on peppers (9 trials) and tomatoes (12 trials) following three broadcast foliar applications of end-use product BSN 2060 240 SC. Pepper trial sites were in regions 2 (GA; 1 trial), 3 (FL; 1 trial), 5 (KS; 1 trial), 6 (TX; 1 trial), 8 (TX; 1 trial), 9 (AZ; 1 trial) and 10 (AZ, CA; 3 trials). Tomato trial sites were in regions 1 (NY; 1 trial), 2 (GA; 1 trial), 3 (FL; 1 trial), 5 (IN; 1 trial) and 10 (CA; 7 trials). The residue decline data indicated a reduction in spiromesifen-derived residues with increasing PHI.

Pepper and tomato trials conducted with the end-use product BSN 2060 240 SC (LOQ = 0.01 ppm)									
Commodity	**Total Applic. Rate kg a.i./ha**	**PHI (days)**	**Residue Levels (ppm)**						
			n	**Min.**	**Max.**	**HAFT**	**Median (STMdR)**	**Mean (STMR)**	**Std. Dev.**
BSN 2060 (parent - Spiromesifen)									
Pepper	0.451–0.494	0	4	0.138	0.256	0.214	0.168	0.182	0.05
		7	18	<0.01	0.118	0.105	0.032	0.04	0.03
		14	18	<0.01	0.092	0.07	0.012	0.023	0.02
		21	4	0.01	0.041	0.03	0.02	0.024	0.01
		28	4	<0.01	0.037	0.03	0.019	0.011	0.01
Tomato	0.447–0.462	0	4	0.119	0.205	0.199	0.162	0.162	0.04
		7	24	0.01	0.242	0.226	0.051	0.065	0.06
		14	24	<0.01	0.189	0.176	0.029	0.042	0.05
		21	4	<0.01	0.02	0.02	0.015	0.015	<0.01
		28	4	<0.01	0.015	0.01	0.01	0.011	<0.01
BSN 2060-enol (metabolite)									
Pepper	0.451–0.494	0	4	0.01	0.06	0.06	0.037	0.036	0.03
		7	18	<0.01	0.02	0.02	0.01	0.011	<0.01
		14	18	<0.01	<0.01	<0.01	0.01	0.01	0
		21	4	<0.01	<0.01	<0.01	0.01	0.01	0
		28	4	<0.01	<0.01	<0.01	0.01	0.01	0
Tomato	0.447–0.462	0	4	0.01	0.024	0.02	0.019	0.018	<0.01
		7	24	<0.01	0.01	<0.01	0.01	0.01	0
		14	24	<0.01	0.01	<0.01	0.01	0.01	0
		21	4	<0.01	<0.01	<0.01	0.01	0.01	0
		28	4	<0.01	<0.01	<0.01	0.01	0.01	0
Total Spiromesifen Residues									
Pepper	0.451–0.494	0	4	0.182	0.273	0.228	0.209	0.218	0.04
		7	18	<0.02	0.138	0.122	0.043	0.05	0.03
		14	18	<0.02	<0.102	<0.076	0.022	0.033	0.02
		21	4	<0.023	<0.051	<0.042	0.03	0.034	0.01
		28	4	<0.02	<0.047	<0.043	0.029	0.031	0.01
Tomato	0.447–0.462	0	4	0.134	0.23	0.223	0.179	0.181	0.05
		7	24	<0.021	<0.252	<0.236	0.061	0.076	0.06
		14	24	<0.02	<0.199	<0.186	0.039	0.052	0.05
		21	4	<0.02	<0.03	<0.03	0.025	0.025	<0.01
		28	4	<0.02	<0.025	<0.023	0.02	0.021	<0.01

CROP FIELD TRIALS ON BROCCOLI AND CABBAGE	PMRA # 1296177

During the 2000 and 2001 broccoli and cabbage growing seasons, field trials were conducted at 12 locations to evaluate the magnitude of residue in/on broccoli (6 trials) and cabbages (6 trials) following three foliar applications of end-use product BSN 2060 240 SC. Broccoli trial sites were in regions 6 (TX; 1 trial), 10 (CA; 4 trials) and 12 (OR; 1 trial). Cabbage trial sites were in regions 1 (PA; 1 trial), 2 (GA; 1 trial), 3 (FL; 1 trial), 5 (IA; 1 trial), 6 (TX; 1 trial) and 10 (CA; 1 trial). At longer PHIs, residues declined in broccoli, but did not decline in cabbage.

Broccoli and cabbage trials conducted with the end-use product BSN 2060 240 SC (LOQ = 0.01 ppm)

Commodity	Total Applic. Rate kg a.i./ha	PHI (days)	Residue Levels (ppm)						
			n	Min.	Max.	HAFT	Median (STMdR)	Mean (STMR)	Std. Dev.
BSN 2060 (parent - Spiromesifen)									
Broccoli	0.445–0.462	0	2	0.434	0.638	0.536	0.536	0.536	0.144
		5–9	12	<0.01	0.669	0.534	0.14	0.181	0.185
		10	2	0.05	0.062	0.06	0.057	0.057	<0.01
		14–16	12	<0.01	0.298	0.238	0.016	0.066	0.09
		22	2	0.01	0.014	0.01	0.013	0.013	<0.01
BSN 2060-enol (metabolite)									
Broccoli	0.445–0.462	0	2	0.01	0.017	0.02	0.015	0.015	<0.01
		5–9	12	<0.01	0.044	0.04	0.019	0.021	0.01
		10	2	<0.01	<0.01	0.01	0.01	0.01	0
		14–16	12	<0.01	0.027	0.03	0.01	0.013	<0.01
		22	2	<0.01	<0.01	0.01	0.01	0.01	0
Total Spiromesifen Residues									
Broccoli	0.445–0.462	0	2	0.447	0.655	0.551	0.551	0.551	0.147
		5–9	12	<0.020	0.713	0.574	0.17	0.212	0.194
		10	2	<0.061	<0.072	0.07	0.067	0.067	<0.01
		14–16	12	<0.020	0.325	0.264	0.026	0.079	0.1
		22	2	<0.021	<0.024	0.02	0.023	0.023	<0.01
BSN 2060 (parent - Spiromesifen)									
Cabbage	0.451–0.466	0	2	0.426	0.486	0.456	0.456	0.456	0.04
		6–9	12	<0.01	1.64	1.54	0.339	0.523	0.56
		13–15	12	<0.01	1.43	1.4	0.19	0.466	0.522
		21	2	1.07	1.12	1.1	1.095	1.095	0.04
		28	2	0.536	0.714	0.625	0.625	0.625	0.126

BSN 2060-enol (metabolite)									
Cabbage	0.451–0.466	0	2	0.109	0.138	0.124	0.124	0.124	0.02
		6–9	12	<0.01	0.275	0.273	0.061	0.087	0.09
		13–15	12	<0.01	0.209	0.209	0.037	0.078	0.08
		21	2	0.104	0.132	0.118	0.118	0.118	0.02
		28	2	0.09	0.086	0.09	0.086	0.086	<0.01
Total Spiromesifen Residues									
Cabbage	0.451 - 0.466	0	2	0.535	0.624	0.58	0.58	0.58	0.06
		6–9	12	<0.02	1.91	1.815	0.387	0.61	0.646
		13–15	12	<0.02	1.603	1.557	0.224	0.545	0.591
		21	2	1.174	1.252	1.213	1.213	1.213	0.06
		28	2	0.621	0.8	0.711	0.711	0.711	0.127

CROP FIELD TRIALS ON CANTALOUPE, CUCUMBER AND SUMMER SQUASH — **PMRA # 1296174**

During the 2000 and 2001 growing seasons, field trials were conducted at 17 locations to evaluate the magnitude of residue in/on cantaloupe (6 trials), cucumber (6 trials) and summer squash (5 trials) following three foliar applications of the end-use product BSN 2060 240 SC. Cantaloupe trial sites were in regions 2 (GA; 1 trial), 5 (IN; 1 trial), 6 (TX; 1 trial) and 10 (AZ, CA; 3 trials). Cucumber trial sites were in regions 2 (GA; 2 trials), 3 (FL; 1 trial), 5 (MN, IN; 2 trials) and 6 (TX; 1 trial). Summer squash trial sites were in regions 1 (NY; 1 trial), 2 (GA; 1 trial), 3 (FL; 1 trial), 5 (IN; 1 trial) and 10 (CA; 1 trial). Spiromesifen-derived residues on cantaloupe, cucumbers and summer squash declined with increasing PHIs.

Cantaloupe, cucumber and summer squash trials conducted with the end-use product BSN 2060 240 SC
(LOQ = 0.01 ppm)

Commodity	**Total Applic. Rate kg a.i./ha**	**PHI (days)**	**Residue Levels (ppm)**						
			n	**Min.**	**Max.**	**HAFT**	**Median (STMdR)**	**Mean (STMR)**	**Std. Dev.**
BSN 2060 (parent - Spiromesifen)									
Cucumber	0.455	0	2	0.03	0.032	0.03	0.029	0.029	<0.01
	0.448–0.459	7	12	<0.01	0.012	<0.011	0.01	0.0103	<0.01
		12–14	12	<0.01	<0.01	<0.01	0.01	0.01	0
	0.455	19	2	<0.01	<0.01	<0.01	0.01	0.01	0
		26	2	<0.01	<0.01	<0.01	0.01	0.01	0
BSN 2060-enol (metabolite)									
Cucumber	0.455	0	2	0.02	0.024	0.02	0.024	0.024	<0.01
	0.448–0.459	7	12	<0.01	0.027	0.03	0.019	0.019	<0.01
		12–14	12	<0.01	0.015	0.01	0.01	0.011	<0.01
	0.455	19	2	<0.01	<0.01	<0.01	0.01	0.01	0
		26	2	<0.01	<0.01	<0.01	0.01	0.01	0

Total Spiromesifen Residues									
Cucumber	0.455	0	2	0.05	0.056	0.05	0.053	0.053	<0.01
	0.448–0.459	7	12	<0.02	0.037	<0.037	0.031	0.029	<0.01
		12–14	12	<0.02	0.025	<0.024	0.02	0.021	<0.01
	0.455	19	2	<0.02	<0.02	<0.02	0.02	0.02	0
		26	2	<0.02	<0.02	<0.02	0.02	0.02	0
BSN 2060 (parent - Spiromesifen)									
Cantaloupe	0.456	0	2	0.09	0.109	0.1	0.097	0.097	0.02
	0.442–0.459	7–9	12	0.01	0.062	0.06	0.019	0.025	0.02
		13–15	12	<0.01	0.038	0.04	0.01	0.016	0.01
	0.456	21	2	0.01	0.025	0.02	0.018	0.018	<0.01
		23	2	<0.01	0.015	0.01	0.013	0.013	<0.01
BSN 2060-enol (metabolite)									
Cantaloupe	0.456	0	2	0.01	0.014	0.01	0.013	0.013	<0.01
	0.442–0.459	7–9	12	<0.01	0.01	0.01	0.01	0.01	0
		13–15	12	<0.01	0.01	<0.01	0.01	0.01	0
	0.456	21	2	<0.01	<0.01	<0.01	0.01	0.01	0
		23	2	<0.01	<0.01	<0.01	0.01	0.01	0
Total Spiromesifen Residues									
Cantaloupe	0.456	0	2	0.1	0.123	0.11	0.11	0.11	0.02
	0.442–0.459	7–9	12	<0.021	0.072	0.07	0.03	0.035	0.02
		13–15	12	<0.02	0.048	<0.045	0.02	0.026	0.01
	0.456	21	2	<0.021	<0.035	<0.028	0.028	0.028	<0.01
		23	2	<0.020	<0.025	<0.023	0.023	0.023	<0.01
BSN 2060 (parent - Spiromesifen)									
Summer Squash	0.458	0	2	0.121	0.139	0.13	0.13	0.13	0.01
	0.446–0.458	7–8	10	<0.01	0.022	0.02	0.011	0.012	<0.01
		11–14	10	<0.01	0.017	0.02	0.01	0.011	<0.01
	0.458	21	2	<0.01	<0.01	<0.01	0.01	0.01	0
		28	2	<0.01	<0.01	<0.01	0.01	0.01	0
BSN 2060-enol (metabolite)									
Summer Squash	0.458	0	2	0.03	0.038	0.03	0.034	0.034	<0.01
	0.446–0.458	7– 8	10	<0.01	0.035	0.03	0.01	0.014	<0.01
		11–14	10	<0.01	0.016	0.01	0.01	0.011	<0.01
	0.458	21	2	<0.01	<0.01	<0.01	0.01	0.01	0
		28	2	<0.01	<0.01	<0.01	0.01	0.01	0

Total Spiromesifen Residues									
Summer Squash	0.458	0	2	0.152	0.177	0.165	0.165	0.165	0.02
	0.446–0.458	7–8	10	<0.02	0.052	0.05	0.021	0.027	0.01
		11–14	10	<0.02	0.033	0.03	0.02	0.022	<0.01
	0.458	21	2	<0.02	<0.02	<0.02	0.02	0.02	0
		28	2	<0.02	<0.02	<0.02	0.02	0.02	0

CROP FIELD TRIALS ON HEAD LETTUCE, LEAF LETTUCE AND SPINACH | **PMRA # 1296178**

During the 2000 and 2001 growing seasons, field trials were conducted at 18 locations to evaluate the magnitude of residue in/on head lettuce (6 trials), leaf lettuce (6 trials) and spinach (6 trials) following three foliar applications of the end-use product BSN 2060 240 SC. Head lettuce trial sites were in regions 1 (NY; 1 trial), 3 (FL; 1 trial) and 10 (AZ, CA; 4 trials). Leaf lettuce trial sites were in regions 1 (NY; 1 trial), 3 (FL; 1 trial) and 10 (AZ, CA; 4 trials). Spinach trial sites were in regions 1 (PA; 1 trial), 2 (VA; 1 trial), 6 (TX; 1 trial), 9 (AZ; 1 trial) and 10 (AZ, CA; 2 trials). Data from the residue decline trial indicate that spiromesifen-derived residues decreased in head lettuce, leaf lettuce and generally declined in spinach with increasing PHIs.

Head lettuce, leaf lettuce and spinach trials conducted with the end-use product BSN 2060 240 SC (LOQ = 0.01 ppm)

Commodity	**Total Applic. Rate kg a.i./ha**	**PHI (days)**	**Residue Levels (ppm)**						
			n	**Min.**	**Max.**	**HAFT**	**Median (STMdR)**	**Mean (STMR)**	**Std. Dev.**
BSN 2060 (parent - Spiromesifen)									
Head Lettuce	0.451	0	2	1.98	2.4	2.19	2.19	2.19	0.297
	0.451–0.465	6–9	12	0.132	4.25	4.12	1.07	1.53	1.38
		12–14	12	<0.01	2.68	2.45	0.453	0.727	0.845
	0.451	20	2	0.285	0.339	0.312	0.312	0.312	0.04
		28	2	0.12	0.275	0.197	0.198	0.198	0.11
BSN 2060-enol (metabolite)									
Head Lettuce	0.451	0	2	0.144	0.152	0.148	0.148	0.148	<0.01
	0.451–0.465	6–9	12	0.02	0.4	0.357	0.121	0.145	0.113
		12–14	12	<0.01	0.359	0.333	0.069	0.113	0.111
	0.451	20	2	0.02	0.027	0.03	0.026	0.026	<0.01
		28	2	<0.01	0.02	0.02	0.015	0.015	<0.01
Total Spiromesifen Residues									
Head Lettuce	0.451	0	2	2.12	2.55	2.34	2.34	2.34	0.304
	0.451–0.465	6–9	12	0.156	4.65	4.48	1.19	1.68	1.49
		12–14	12	<0.01	2.99	2.79	0.551	0.84	0.947
	0.451	20	2	0.312	0.363	0.338	0.338	0.338	0.04
		28	2	0.129	0.295	0.212	0.212	0.212	0.117

BSN 2060 (parent - Spiromesifen)									
Leaf Lettuce	0.458	0	2	4.48	4.84	4.66	4.66	4.66	0.255
	0.451–0.466	7–8	12	0.445	9.46	8.74	1.15	2.43	3.03
		13–14	12	0.02	4.05	3.65	0.16	0.874	1.37
	0.458	21	2	0.897	1.4	1.15	1.15	1.15	0.356
		28	2	0.477	0.669	0.573	0.573	0.573	0.136
BSN 2060-enol (metabolite)									
Leaf Lettuce	0.458	0	2	0.193	0.203	0.198	0.198	0.198	<0.01
	0.451–0.466	7–8	12	0.06	0.529	0.515	0.109	0.21	0.178
		13–14	12	<0.01	0.317	0.289	0.033	0.076	0.102
	0.458	21	2	0.05	0.059	0.06	0.056	0.056	<0.01
		28	2	0.04	0.047	0.04	0.043	0.043	<0.01
Total Spiromesifen Residues									
Leaf Lettuce	0.458	0	2	4.68	5.03	4.86	4.86	4.86	0.247
	0.451–0.466	7–8	12	0.507	9.99	9.25	1.37	2.64	3.18
		13–14	12	0.03	4.37	3.94	0.194	0.95	1.47
	0.458	21	2	0.949	1.46	1.2	1.2	1.2	0.361
		28	2	0.524	0.709	0.617	0.617	0.617	0.131
BSN 2060 (parent - Spiromesifen)									
Spinach	0.449	0	2	6.86	7.32	7.09	7.09	7.09	0.325
	0.449–0.476	6–9	12	0.14	8.35	7.05	3.31	3.53	2.61
		13–14	12	0.07	4.9	4.36	0.464	1.6	1.96
BSN 2060-enol (metabolite)									
Spinach	0.449	0	2	0.274	0.303	0.289	0.289	0.289	0.02
	0.449–0.476	6–9	12	0.09	0.91	0.85	0.233	0.308	0.27
		13–14	12	0.01	0.813	0.726	0.05	0.17	0.267
Total Spiromesifen Residues									
Spinach	0.449	0	2	7.14	7.63	7.39	7.39	7.39	0.346
	0.449–0.476	6–9	12	0.236	8.65	7.33	3.45	3.83	2.75
		13–14	12	0.111	5.72	5.09	0.515	1.77	2.18

CROP FIELD TRIALS ON COTTON **PMRA # 1296176**

During the 2000 and 2001 cotton growing season, field trials were conducted at 12 locations to evaluate the magnitude of residue in/on cottonseed and cotton byproducts following two foliar applications of end-use product BSN 2060 240 SC. Cotton trial sites were in regions 2 (GA; 1 trial), 4 (MS, AR; 3 trials), 6 (OK; 1 trial), 8 (OK, TX; 4 trials) and 10 (AZ, CA; 3 trials). Residue decline data indicated a decrease in spiromesifen-derived residues by the 28-35 day PHI.

Cotton trials conducted with the end-use product BSN 2060 240 SC (LOQ = 0.01 ppm)

Commodity	Total Applic. Rate kg a.i./ha	PHI (days)	Residue Levels (ppm)						
			n	Min.	Max.	HAFT	Median (STMdR)	Mean (STMR)	Std. Dev.
BSN 2060 (parent - Spiromesifen)									
Cottonseed	0.551–0.578	28–35	24	<0.01	0.241	0.2	0.019	0.066	0.07
Cotton Byproducts			12	0.157	9.5	8.42	1.45	3.03	3.02
BSN 2060-enol (metabolite)									
Cottonseed	0.551–0.578	28–35	24	<0.01	0.503	0.19	0.032	0.078	0.111
Cotton Byproducts			12	0.155	2.81	2.72	1.05	1.187	0.823
Total Spiromesifen Residues									
Cottonseed	0.551–0.578	28–35	24	<0.02	0.459	0.39	0.086	0.133	0.133
Cotton Byproducts			12	0.312	12.31	11.13	2.665	4.218	3.758

CROP FIELD TRIALS ON GREENHOUSE-GROWN CUCUMBER — **PMRA # 1296186 and 1296187**

During the 1999 growing season, greenhouse trials were conducted in Europe at 7 locations to evaluate the magnitude of residue in/on greenhouse-grown cucumbers following four foliar applications of the end-use product BSN 2060 240 SC. Cucumber trial sites were in Spain (1 trial), Greece (1 trial), Italy (1 trial), France (1 trial), Belgium (1 trial), the Netherlands (1 trial) and the Federal Republic of Germany (2 trials). Data from the residue decline trial indicate that spiromesifen-derived residues decreased in/on greenhouse-grown cucumber with increasing PHIs.

Greenhouse-grown cucumber trials conducted with the end-use product BSN 2060 240 SC (LOQ = 0.01 ppm)

Commodity	Total Applic. Rate kg a.i./ha	PHI (days)	Residue Levels (ppm)						
			n	Min.	Max.	HAFT	Median (STMdR)	Mean (STMR)	Std. Dev.
BSN 2060 (parent - Spiromesifen)									
Cucumber, fruit	0.494–0.930	0	8	0.03	0.126	0.126	0.059	0.065	0.03
		1	4	0.03	0.122	0.122	0.053	0.063	0.04
		3	8	0.02	0.111	0.111	0.031	0.039	0.03
		7	8	<0.01	0.089	0.09	0.015	0.024	0.03
		10	4	<0.01	0.054	0.05	0.013	0.023	0.02

BSN 2060-enol (metabolite)									
Cucumber, fruit	0.494–0.930	0	8	0.01	0.03	0.03	0.02	0.021	<0.01
		1	4	0.01	0.03	0.03	0.019	0.019	<0.01
		3	8	<0.01	0.033	0.03	0.018	0.019	<0.01
		7	8	<0.01	0.023	0.02	0.016	0.015	<0.01
		10	4	<0.01	0.014	0.01	0.012	0.012	<0.01
Total Spiromesifen Residues									
Cucumber, fruit	0.494–0.930	0	8	0.04	0.143	0.143	0.085	0.086	0.03
		1	4	0.04	0.138	0.138	0.078	0.083	0.04
		3	8	<0.029	0.126	0.126	0.049	0.058	0.03
		7	8	0.02	0.105	0.105	0.029	0.039	0.03
		10	4	<0.02	0.068	0.07	0.025	0.035	0.02

CROP FIELD TRIALS ON GREENHOUSE-GROWN TOMATO — **PMRA # 1296168, 1269169, 1296185**

During the 1999 and 2004 growing seasons, greenhouse trials were conducted in Europe at 8 locations to evaluate the magnitude of residue in/on greenhouse-grown tomato following four foliar applications of the end-use product BSN 2060 240 SC. During the 1999 growing season, tomato trial sites were in Belgium (1 trial), France (1 trial), Germany (2 trials), Italy (1 trial), the Netherlands (1 trial), Portugal (1 trial) and Spain (1 trial). Eight additional trials on cherry tomatoes were conducted during the 2004 growing season at trials sites in Belgium (1 trial), the Netherlands (1 trial), Spain (2 trials), Italy (2 trials), Greece (1 trial) and France (1 trial). Data from the residue decline trial indicate that total spiromesifen residues decreased in/on greenhouse-grown tomato with increasing PHIs.

Greenhouse-grown tomato trials conducted with the end-use product BSN 2060 240 SC (LOQ = 0.01 ppm)

Commodity	**Total Applic. Rate kg a.i./ha**	**PHI (days)**	**Residue Levels (ppm)**						
			n	**Min.**	**Max.**	**HAFT**	**Median (STMdR)**	**Mean (STMR)**	**Std. Dev.**
BSN 2060 (parent - Spiromesifen)									
Tomato, fruit	0.562–0.864	0–1	24	0.07	0.52	0.52	0.16	0.211	0.132
		3	18	0.05	0.48	0.48	0.154	0.176	0.11
		6–7	12	0.03	0.35	0.35	0.099	0.129	0.1
		10	8	0.03	0.25	0.25	0.08	0.112	0.08
BSN 2060-enol (metabolite)									
Tomato, fruit	0.562–0.864	0–1	24	<0.01	0.015	0.02	0.01	0.011	<0.01
		3	18	<0.01	0.014	0.01	0.01	0.01	<0.01
		6–7	12	<0.01	0.018	0.02	0.01	0.011	<0.01
		10	8	<0.01	0.011	0.01	0.01	0.01	0
Total Spiromesifen Residues									

Tomato, fruit	0.562–0.864	0–1	24	<0.08	0.535	0.535	0.17	0.222	0.133
		3	18	<0.061	0.494	0.494	0.164	0.186	0.111
		6–7	12	<0.04	0.368	0.368	0.109	0.14	0.1
		10	8	<0.04	0.261	0.261	0.09	0.122	0.08

CROP FIELD TRIALS ON GREENHOUSE-GROWN PEPPER — **PMRA # 1296170, 1296171, 1296187**

During the 1999-2000 and 2004 growing seasons, greenhouse trials were conducted in Europe at four locations to evaluate the magnitude of residue in/on greenhouse-grown pepper following four foliar applications of the end-use product BSN 2060 240 SC. Pepper trial sites were in Belgium (1 trial), Germany (2 trials), Italy (1 trial) and the Netherlands (2 trials). Data from the residue decline trial indicated that spiromesifen-derived residues generally declined in/on greenhouse-grown pepper with increasing PHIs.

Greenhouse-grown pepper trials conducted with the end-use product BSN 2060 240 SC (LOQ = 0.01 ppm)

Commodity	**Total Applic. Rate kg a.i./ha**	**PHI (days)**	**Residue Levels (ppm)**						
			n	**Min.**	**Max.**	**HAFT**	**Median (STMdR)**	**Mean (STMR)**	**Std. Dev.**
BSN 2060 (parent - Spiromesifen)									
Pepper, fruit	0.303–0.842	0–1	9	0.06	0.231	0.231	0.17	0.145	0.07
		3	6	0.07	0.174	0.174	0.103	0.106	0.04
		6–7	5	0.04	0.149	0.149	0.053	0.082	0.05
		10	3	0.03	0.06	0.06	0.046	0.045	0.02
BSN 2060-enol (metabolite)									
Pepper, fruit	0.303–0.842	0–1	9	<0.01	0.025	0.03	0.01	0.015	<0.01
		3	6	<0.01	0.019	0.02	0.01	0.013	<0.01
		6–7	5	<0.01	0.016	0.02	0.01	0.012	<0.01
		10	3	<0.01	<0.01	<0.01	0.01	0.01	<0.01
Total Spiromesifen Residues									
Pepper, fruit	0.303–0.842	0–1	9	<0.074	0.256	0.256	0.18	0.16	0.07
		3	6	<0.075	0.193	0.193	0.113	0.118	0.04
		6–7	5	<0.046	0.165	0.165	0.065	0.093	0.05
		10	3	<0.039	<0.07	0.07	0.056	0.055	0.02

FIELD ACCUMULATION IN ROTATIONAL CROPS - ALFALFA — **PMRA # 1296285**

For **alfalfa**, three applications were made to bare ground at use rates of 272 to 287 g a.i./ha per application with 0- to 13-day retreatment intervals (RTIs), for maximum use rates of 827 to 843 g a.i./ha. Twenty-four to 31 days following the third application, the soil was tilled and the alfalfa was planted to simulate an immediate (30-day) plant-back interval (PBI).

Commodity	Total Rate (kg a.i./ha)	Plant-back Interval (days)	Residue Levels (ppm)						
			n	Min.	Max.	HAFT	Median (STMdR)	Mean (STMR)	Std. Dev.
BSN 2060 (parent - Spiromesifen)									
Alfalfa Forage	0.827 to 0.843	24 to 31	24	<0.001	<0.001	<0.001	<0.001	<0.001	0
Alfalfa Hay	0.827 to 0.843	24 to 31	24	<0.005	<0.005	<0.005	<0.005	<0.005	0
BSN 2060-enol (metabolite)									
Alfalfa Forage	0.827 to 0.843	24 to 31	24	<0.001	<0.001	<0.001	<0.001	<0.001	0
Alfalfa Hay	0.827 to 0.843	24 to 31	24	<0.005	<0.005	<0.005	<0.005	<0.005	0
BSN 2060 4-hydroxymethyl									
Alfalfa Forage	0.827 to 0.843	24 to 31	24	<0.004	1.0744	0.854	0.0855	0.1767	0.247
Alfalfa Hay	0.827 to 0.843	24 to 31	24	<0.013	2.2765	2.22	0.2947	0.5197	0.632
Total Spiromesifen Residues									
Alfalfa Forage	0.827 to 0.843	24 to 31	24	<0.004	1.0744	0.854	0.0855	0.1767	0.247
Alfalfa Hay	0.827 to 0.843	24 to 31	24	<0.013	2.2765	2.22	0.2947	0.5197	0.632

FIELD ACCUMULATION IN ROTATIONAL CROPS - SUGAR BEET	**PMRA #1296288**

For **sugar beet**, three applications were made to bare ground at a use rate of 270 to 292 g a.i./ha per application with 0- to 10-day retreatment intervals (RTIs), for a maximum use rate of 833-864 g a.i./ha. Twenty-six to 34 days following the third application, the soil was tilled and the sugar beets planted to simulate an immediate (30-day) plant-back interval (PBI).

Commodity	Total Rate (kg a.i./ha)	Plant-back Interval (days)	Residue Levels (ppm)						
			n	Min.	Max.	HAFT	Median (STMdR)	Mean (STMR)	Std. Dev.
BSN 2060 (parent - Spiromesifen)									
Sugar Beet Root	0.833 to 0.864	26 to 34	24	<0.001	<0.002	<0.02	<0.002	<0.002	NA
Sugar Beet Top	0.833 to 0.864	26 to 34	24	<0.001	<0.001	<0.02	<0.001	<0.001	NA
BSN 2060-enol (metabolite)									
Sugar Beet Root	0.833 to 0.864	26 to 34	24	<0.001	<0.002	<0.02	<0.002	<0.002	NA
Sugar Beet Top	0.833 to 0.864	26 to 34	24	<0.001	<0.001	<0.02	<0.001	<0.001	NA

BSN 2060 4-hydroxymethyl									
Sugar Beet Root	0.833 to 0.864	26 to 34	24	<0.006	0.007	<0.02	<0.003	<0.003	NA
Sugar Beet Top	0.833 to 0.864	26 to 34	24	<0.004	0.171	0.16	0.005	0.018	0.044
Total Spiromesifen Residues									
Sugar Beet Root	0.833 to 0.864	26 to 34	24	<0.006	0.007	<0.02	<0.003	<0.003	NA
Sugar Beet Top	0.833 to 0.864	26 to 34	24	<0.004	0.171	0.16	0.005	0.018	0.044

FIELD ACCUMULATION IN ROTATIONAL CROPS - WHEAT — **PMRA # 1296292**

For winter and spring **wheat**, three applications were made to bare ground at a use rate of 270 to 292 g a.i./ha per application with 0- to 8-day retreatment intervals (RTIs), for a maximum use rate of 830-853 g a.i./ha. Twenty-seven to 39 days following the third application, the soil was tilled and the wheat was planted to simulate an immediate (30-day) plant-back interval (PBI).

Commodity	**Total Rate (kg a.i./ha)**	**Plant-back Interval (days)**	**Residue Levels (ppm)**						
			n	**Min.**	**Max.**	**HAFT**	**Median (STMdR)**	**Mean (STMR)**	**Std. Dev.**
BSN 2060 (parent - Spiromesifen)									
Wheat Forage	0.797 to 0.843	27–39	40	<0.003	<0.003	<0.01	<0.003	<0.003	NA
Wheat Hay	0.797 to 0.843	27–39	40	<0.003	<0.003	<0.01	<0.003	<0.003	NA
Wheat Straw	0.797 to 0.843	27–39	40	<0.001	<0.001	<0.01	<0.001	<0.001	NA
Wheat Grain	0.797 to 0.843	27–39	40	<0.001	<0.001	<0.01	<0.001	<0.001	NA
BSN 2060-enol (metabolite)									
Wheat Forage	0.797 to 0.843	27–39	40	<0.003	0.005	<0.02	<0.003	0.0031	0
Wheat Hay	0.797 to 0.843	27–39	40	<0.003	0.004	<0.02	<0.003	0.003	0
Wheat Straw	0.797 to 0.843	27–39	40	<0.001	0.006	<0.01	<0.001	0.0011	0
Wheat Grain	0.797 to 0.843	27–39	40	<0.001	<0.001	<0.01	<0.001	<0.001	NA
BSN 2060 4-hydroxymethyl									
Wheat Forage	0.797 to 0.843	27–39	40	<0.006	0.1468	0.14	0.0171	0.0324	0.035
Wheat Hay	0.797 to 0.843	27–39	40	<0.009	0.1043	0.1	0.0375	0.0437	0.033

Wheat Straw	0.797 to 0.843	27–39	40	<0.013	0.2133	0.21	0.0293	0.0452	0.049
Wheat Grain	0.797 to 0.843	27–39	40	<0.004	0.009	<0.01	0.004	0.0044	0
Total Spiromesifen Residues									
Wheat Forage	0.797 to 0.843	27–39	40	<0.02	0.147	0.14	0.02	0.038	0.032
Wheat Hay	0.797 to 0.843	27–39	40	<0.02	0.104	0.1	0.0375	0.047	0.03
Wheat Straw	0.797 to 0.843	27–39	40	<0.01	0.213	0.21	0.0295	0.0475	0.047
Wheat Grain	0.797 to 0.843	27–39	40	<0.01	<0.01	<0.01	<0.01	<0.01	NA

FIELD ACCUMULATION IN ROTATIONAL CROPS - BARLEY | **PMRA # 1296293**

For **barley**, three applications were made to bare ground at a use rate of 258 to 292 g a.i./ha per application with 0- to 8-day retreatment intervals (RTIs), for a maximum use rate of 822-878 g a.i./ha. Twenty-seven to 31 days following the third application, the soil was tilled and the barley was planted to simulate an immediate (30-day) plant-back interval (PBI).

Commodity	**Total Rate (kg a.i./ha)**	**Plant-back Interval (days)**	**Residue Levels (ppm)**						
			n	**Min.**	**Max.**	**HAFT**	**Median (STMdR)**	**Mean (STMR)**	**Std. Dev.**
BSN 2060 (parent - Spiromesifen)									
Barley Hay	0.836–0.855	27–31	24	<0.002	<0.002	<0.02	<0.002	<0.002	NA
Barley Straw	0.836–0.855	27–31	24	<0.001	<0.001	<0.02	<0.001	<0.001	NA
Barley Grain	0.836–0.855	27–31	24	<0.001	<0.001	<0.02	<0.001	<0.001	NA
BSN 2060-enol (metabolite)									
Barley Hay	0.836–0.855	27–31	24	<0.001	0.002	<0.02	<0.001	0.001	0
Barley Straw	0.836–0.855	27–31	24	<0.001	<0.001	<0.02	<0.001	<0.001	NA
Barley Grain	0.836–0.855	27–31	24	<0.001	<0.001	<0.02	<0.001	<0.001	NA
BSN 2060 4-hydroxymethyl									
Barley Hay	0.836–0.855	27–31	24	<0.016	0.2311	0.18	0.056	0.073	0.056
Barley Straw	0.836-0.855	27–31	24	<0.005	0.12	0.11	0.03	0.042	0.031
Barley Grain	0.836-0.855	27–31	24	<0.004	0.0119	<0.02	<0.004	<0.004	NA

Total Spiromesifen Residues									
Barley Hay	0.836–0.855	27–31	24	<0.02	0.2311	0.18	0.056	0.073	0.056
Barley Straw	0.836–0.855	27–-31	24	<0.02	0.12	0.11	0.03	0.042	0.031
Barley Grain	0.836–0.855	27–31	24	<0.01	0.0119	<0.02	<0.004	<0.004	NA

PROCESSED FOOD AND FEED	**PMRA # 1296280 (wheat), #1296286 (cottonseed), #1296279 (corn), #1296291 (sugar beet), #1296278 (potato), #1296284 (field tomato), #1296277 (greenhouse tomatoes)**

Field Tomatoes: In one field trial in CA (EPA Growing Region 10), tomatoes were harvested 16-day following the last of three applications of the SC formulation (BSN 2060 240 SC) at approximately 0.46 kg a.i./ha/application, with a 7-day retreatment interval, for a total rate of 1.38 kg a.i./ha. The final application was made at the third fruit cluster stage.

Processed Commodity	*Processing Factor*
Paste	2.3
Puree	<1
Canned Tomatoes	<1
Juice	<1
Hot Crushed Tomatoes	<1
Dried Tomatoes	4.8

Greenhouse Tomatoes: In two field trials from Europe (1 in Germany, 1 in Belgium), tomatoes were taken at a 3-day preharvest interval (PHI) following 4 foliar spray applications of BSN 2060 240 SC. The tomatoes were treated at approximately 0.216 kg a.i./ha/application, with a 9-11 day retreatment interval (RTI), for a total rate of 0.864 kg a.i./ha. Several stages of fruit development appeared concurrently on the same plant over all applications.

Processed Commodity	*Processing Factor*
Washed Fruit	<1
Washing Water	<1
Peeled Fruit	<1
Peeling Water with Peel	<1
Raw Juice	<1
Juice	<1
Preserve	<1
Wet Pomace	6.9
Puree	1.4

Potato: In one field trial in Idaho (EPA Growing Region 11), potatoes were harvested seven days after the last of two foliar broadcast applications of BSN 2060 240 SC at a rate of approximately 1.38 to 1.47 kg a.i./ha/application, with a seven-day retreatment interval, for a total rate of 2.86 kg a.i./ha. The final application was made when 70% of the tuber mass was achieved. Total spiromesifen residues in the potato tubers treated at 2.86 kg a.i./ha and in each of the potato processed commodities, as well as the washed and cooked tubers, were less than the limit of quantitation (LOQ) (<0.01 ppm). Therefore no processing factors were calculated.

Sugar beet: In one field trial in California (EPA Growing Region 10) sugar beets were planted 27 days following the last of three applications of BSN 2060 240 SC to bare soil at a rate of approximately 1.4 kg a.i./ha/application, with a 7-day retreatment interval (RTI), for a total rate of 4.18 kg a.i./ha. Sugar beet is a rotational crop, so all applications of the EP were made to bare soil.

Processed Commodity	*Processing Factor*
Refined Sugar	<1
Molasses	4.4
Dried Pulp	<1

Corn: In one field trial in Kansas (EPA Growing Region 5), field corn grain was harvested 31 days following the last of two applications of BSN 2060 240 SC at a rate of 0.75 kg a.i./ha/application, with a 13-day retreatment interval (RTI), for a total rate of 1.50 kg a.i./ha. The final application was made at physiological maturity. Since the total spiromesifen and BSN 2060-enol residue on the corn grain treated at 1.50 kg a.i./ha was <LOQ, no processing factors were calculated.

Cottonseed: In two field trials conducted in Mississippi (EPA Growing Region 4), cotton was harvested 28 days following the last of two applications of BSN 2060 240 SC at rates of 1.37 to 1.67 kg a.i./ha, with a 6-8 day retreatment interval (RTI), for a total rate of 3.04–3.05 kg a.i./ha. The final applications were made when 10–20% of the bolls were open.

Processed Commodity	*Processing Factor*
Meal	<1
Oil	<1
Hulls	<1

Wheat: In one field trial in North Dakota (EPA Growing Region 5), wheat was planted 28 days following the last of three applications of BSN 2060 240 SC to bare soil, at a rate of approximately 0.84 kg a.i./ha/application, for a total rate of 2.52 kg a.i./ha. Wheat is a rotational crop, so all applications of the EP were made to bare soil.

Processed Commodity	*Processing Factor*
Bran	3.8
Flour	<1
Shorts	2.4
Middlings	1.1
Germ	<1

STORAGE STABILITY	**PMRA #1296179 (field crops), #1296292 (rotational crops), #1296273 (greenhouse crops)**

In one study, field crop matrices (corn forage, corn stover, corn grain, mustard green whole leaves, cotton undelinted seed, cotton gin byproducts, potato tuber, potato chips, potato granules/flakes, potato wet peel, tomato whole fruit, tomato paste and tomato puree) were spiked at 0.20 ppm with a mixed standard containing spiromesifen and BSN 2060-enol at a 1:1 ratio expressed in parent equivalents (0.10 ppm per analyte). Samples were analysed at 0, 156–160 and 316–347 days. Total spiromesifen residues (spiromesifen + BSN 2060-enol) declined ≤10% in all crops over the entire storage period.

In another study, rotational crop matrices (wheat forage, wheat grain, wheat straw, sugar beet roots and sugar beet tops) were spiked at 0.10 ppm with BSN 2060 4-hydroxymethyl as expressed in parent equivalents. Samples were analysed at 434–468 days. Residues of BSN 2060 4-hydroxymethyl declined ≤22% in all crops over the entire storage period.

Matrix	*Storage Interval (days)*	*Percent Decline (total spiromesifen residues)*
Field Crops		
Corn Green Forage	318	None
Corn Stover (Fodder)	326	None
Corn Grain	318	None
Mustard Greens, Whole Leaves	347	6
Cotton Undelinted Seed	318	10
Cotton Gin Byproducts	322	None
Potato Tuber	320	2
Potato Chips	322	6
Potato Granules/Flakes	322	7
Potato Wet Peel	323	4
Tomato Whole Fruit	316	5
Tomato Paste	318	8
Tomato Puree	322	3
Rotational Crops		
Wheat Forage	434	3
Wheat Grain	468	22
Wheat Straw	434	19
Sugar Beet Roots	436	14
Sugar Beet Tops	465	8

Greenhouse Crops

Greenhouse crop matrices (melon peel, cucumber fruit and climbing French bean) were spiked at 0.20 ppm with a mixed standard containing spiromesifen and BSN 2060-enol at a 1:1 ratio expressed in parent equivalents (0.10 ppm per analyte). Samples were analysed at 0, 30, 60, 91-101, 190, 367–374, 546 and 727 days. The data indicated that the decline in total spiromesifen residues (spiromesifen + BSN 2060-enol) was statistically insignificant ($p > 0.05$), indicating stability at $\leq -18^{\circ}C$ for up to 727 days (24 months) in cucumber fruit, melon peel and climbing French bean (bean and pod).

LIVESTOCK FEEDING | **PMRA #1296238**

Spiromesifen was administered orally via gelatin capsule to 10 lactating Holstein cows (three cows at each treatment rate and one control cow) for 29 consecutive days. Dosing was made at 5, 15, or 50 mg/kg feed (on dry weight basis). The average total residues (parent + metabolites), determined for the day -26 milk, skim milk and cream were measured at 0.018, 0.020 and 0.033 ppm, respectively. Using these data, spiromesifen-related residues were calculated to concentrate by a factor of approximately 1.8X from whole milk to cream and were observed to concentrate by 1.1X in the skim milk.

Matrix	Feeding Level (ppm)		Residue Levels (ppm)					
		n	Min.	Max.	Median	Mean	Std. Dev.	R/F Ratio*
TOTAL SPIROMESIFEN RESIDUES								
Whole Milk (days 4–28)	50	30	<0.015	0.024	0.016	0.017	0.002	0.00048
Whole Milk (day 28)	5	3	<0.015	<0.015	<0.015	<0.015	0	
	15	3	<0.015	<0.015	<0.015	<0.015	0	
Skim Milk	50	3	<0.02	<0.02	<0.02	<0.02	0	Not conducted
Cream	50	3	0.023	0.046	0.031	0.033	0.012	Not conducted
Liver	5	3	<0.10	<0.10	<0.10	<0.10	0	0.0022
	15	3	<0.10	<0.10	<0.10	<0.10	0	
	50	3	0.1	0.11	0.1	0.103	0.006	
Kidney	5	3	<0.10	<0.10	<0.10	<0.10	0	0.006
	15	3	0.1	0.15	0.1	0.117	0.029	
	50	3	0.15	0.3	0.16	0.203	0.084	
Muscle	5	3	<0.02	<0.02	<0.02	<0.02	0	0.00048
	15	3	<0.02	<0.02	<0.02	<0.02	0	
	50	3	<0.02	0.021	0.02	0.020	0.001	
Fat	5	3	<0.02	<0.02	<0.02	<0.02	0	0.00256
	15	3	0.032	0.055	0.033	0.04	0.013	
	50	3	0.062	0.128	0.12	0.103	0.036	

*R/F Ratio = Residue/ Feed ratio

Table 6 Food Residue Chemistry Overview of Metabolism Studies and Risk Assessment

PLANT STUDIES	
RESIDUE DEFINITION FOR ENFORCEMENT **Primary crops (lettuce, cotton, tomato)**	Spiromesifen, BSN 2060-enol
Rotational crops (alfalfa, sugar beet, barley, wheat)	Spiromesifen, BSN 2060-enol, BSN 2060-4-hydroxymethyl (free and conjugated)
RESIDUE DEFINITION FOR RISK ASSESSMENT **Primary crops (lettuce, cotton, tomato)**	Spiromesifen, BSN 2060-enol, BSN 2060-4-hydroxymethyl (free and conjugated)
Rotational crops (alfalfa, sugar beet, barley, wheat)	Spiromesifen, BSN 2060-enol, BSN 2060-4-hydroxymethyl (free and conjugated)
METABOLIC PROFILE IN DIVERSE CROPS	Similar in three diverse crops (lettuce, cotton, tomato).
ANIMAL STUDIES	
ANIMALS	**Ruminant**
RESIDUE DEFINITION FOR ENFORCEMENT **Ruminant**	Spiromesifen, BSN 2060-enol (free and conjugated), BSN 2060-4-hydroxymethyl (free and conjugated)
Poultry	Spiromesifen, BSN 2060-enol
RESIDUE DEFINITION FOR RISK ASSESSMENT **Ruminant**	Spiromesifen, BSN 2060-enol (free and conjugated), BSN 2060-4-hydroxymethyl (free and conjugated)
Poultry	Spiromesifen, BSN 2060-enol, BSN 2060-4-carboxy-3-pentanol, BSN 2060-hydroxy-4-carboxy
METABOLIC PROFILE IN ANIMALS	Quantitative and qualitative differences in poultry and ruminants, but does not affect overall profile assessment.
FAT SOLUBLE RESIDUE	Yes

DIETARY RISK FROM FOOD AND WATER			
	POPULATION	**ESTIMATED RISK % of ACCEPTABLE DAILY INTAKE (ADI)**	
		Food Only	**Food and Water**
Refined chronic non-cancer dietary risk **ADI = 0.007 mg/kg bw** **Estimated environmental concentration (EEC) for chronic drinking water) = 16.51 µg a.i./L**	**All infants < 1 year**	22.8	39.1
	Children 1–2 years	76.4	83.8
	Children 3 to 5 years	70.2	77.1
	Children 6–12 years	46.9	51.7
	Youth 13–19 years	35.5	39.1
	Adults 20–49 years	33.7	38.4
	Adults 50+ years	35.2	40.1
	Females 13-49 years	34.2	38.8
	Total population	38.5	43.5
	POPULATION	**ESTIMATED RISK % of ACUTE REFERENCE DOSE (ARfD)**	
		Food Only	**Food and Water**
	An ARfD was not provided because no endpoint of concern attributable to a single dose was identified.		

Table 7 Fate and Behaviour in the Environment

Terrestrial			
Property (study length)	**Test substance**	**Value**	**Comments**
Abiotic transformation			
Hydrolysis (30 d)	spiromesifen	half life: 25°C: pH 4: 48 d; pH 7: 26 d; pH 9: 4.5 d 25°C: pH 4: 2.2 d; pH 7: 1.7 d; pH 9: 0.2 d	Not an important route of transformation at pH 4 and 7, but increases under basic conditions.
Phototransformation on soil (10 d)	spiromesifen	half life: 23.9 d (continuous irradiation); 47.2 d (12 hr light cycle day). Dark control was faster than irradiated.	Not an important route of transformation.

Property (study length)	Test substance	Value	Comments
Biotransformation			
Biotransformation in aerobic soil (up to 365 d)	spiromesifen	Half life sandy loam: 2.8 d; silt: 3.4 d; TX clay loam: 12 d; CA sandy loam: 18 d	Spiromesifen is non-persistent to moderately persistent depending on soil characteristics[a]
Mobility			
Adsorption or desorption in soil	spiromesifen	not stable in $CaCl_2$, could not be performed.	Spiromesifen is probably immobile based on logKow, water solubility and partitioning to sediment [b].
	BSN 2060-enol	K_d ads: 0.0185-0.049 mL/g K_d des: 0.015-0.049 mL/g	BSN 2060-enol is very highly mobile.
	BSN 2060-4-carboxy	K_d ads: 0.065 mL/g	BSN 2060-4-carboxy is very highly mobile.
Soil leaching	spiromesifen	unaged: TGAI remained in top soil layer BSN 2060-enol: was found in leachate	Spiromesifen is not mobile. BSN 2060-enol is mobile.
HPLC	spiromesifen	K_{oc}: 30 900	Spiromesifen is immobile.
Soil TLC	spiromesifen	Rf: 0.0021; estimated K_{oc}: 69, 445	Spiromesifen is immobile.
Field studies			
Field dissipation	Spiromesifen	spiromesifen Half life: 4.5 d; T9/10: 15 d BSN 2060-enol Half life: 18 d; T9/10: 58 d	Spiromesifen is non-persistent and BSN 2060-enol is slightly persistent[a].
Aquatic			
Abiotic transformation			
Hydrolysis	spiromesifen	half life: 25°C: pH 4: 48 d; pH 7: 26 d; pH 9: 4.5 d 25°C: pH 4: 2.2 d; pH 7: 1.7 d; pH 9: 0.2 d	Not an important route of transformation at pH 4 and 7, but increases under basic conditions.
Phototransformation in water (5 d)	spiromesifen	half life: 1.8 hours (continuous); 3.6 hours (12 hr light cycle day)	An important route of transformation.
Phototransformation in water (9 d)	BSN 2060-enol	half life: 198 hours (continuous); 396 hours (12 hr light cycle day)	Not an important route of transformation.

Property (study length)	Test substance	Value	Comments
Biotransformation			
Biotransformation in aerobic water systems (121 d) - study 1	spiromesifen	Half life: system: 4.1 d	Spiromesifen is non-persistent.
Biotransformation in aerobic water systems (90 d) - study 2	spiromesifen	Half life: system: 8 d	Spiromesifen is slightly persistent .
Biotransformation in anaerobic water systems (120 d)	spiromesifen	Half life: water: 5 d; sediment: 19 d; system: 18 d	Spiromesifen is slightly persistent.
Bioaccumulation	spiromesifen	whole fish BCF: 875 to 916	Spiromesifen bioaccumulates and is readily depurated (52% in 1 day).

Classification of Goring et al. 1975.
Classification of McCall et al. 1981.
Classification of McEwan and Stephenson 1979.

Table 8 Toxicity to Non-Target Species

Terrestrial organisms				
Organism	**Exposure**	**Test substance**	**End point value**	**Degree of toxicity[a]**
Invertebrates				
Earthworm	Acute	spiromesifen	LC_{50} > 1000 mg a.i./kg NOEC: 1000 mg a.i./kg	No classification
	Chronic (reproduction)	EUP (Forbid 240 SC; 23% a.i.)	EC_{50}: >0.75 mg a.i./kg NOEL: 0.75 mg a.i./kg	No classification
Bee	Oral	spiromesifen	LD_{50}: 792.4 µg a.i./bee	Relatively non-toxic according to Atkins (1981)
	Contact	spiromesifen	LC_{50}> 200 µg a.i./bee	Relatively non-toxic according to Atkins (1981)
	Oral	EUP (Forbid 240 SC; 23% a.i.)	LD_{50}: 64.1 µg a.i./bee	Relatively non-toxic according to Atkins (1981)

Organism		Exposure	Test substance	End point value	Degree of toxicity[a]
		Contact	EUP (Forbid 240 SC; 23% a.i.)	LC_{50} >200 µg a.i./bee	Relatively non-toxic according to Atkins (1981)
Predators and Parasites	Rove beetle	contact	Forbid 240 SC; 23% a.i.	NOEC (reproduction): 896 g a.i./ha	
	Carabid beetle	contact	Forbid 240 SC; 23% a.i.	LR_{50}: >656.6 g a.i./ha NOEC (pupae consumed): 656.6 g a.i./ha	
	Ladybird beetle	contact	Forbid 240 SC; 23% a.i.	LR_{50}: 41.7 g a.i./ha NOEC (reproduction): 11 g a.i./ha	
	Green lacewing	contact	Forbid 240 SC; 23% a.i.	LR_{50}: >865.4 g a.i./ha NOEC: (reproduction): 865.4 g a.i./ha	
	Predaceous mite	contact	Forbid 240 SC; 23% a.i.	LR_{50}: 64.8 g a.i./ha NOEC (reproduction): 50.4 g a.i./ha	
	Aphid parasitoid	contact	Forbid 240 SC; 23% a.i.	LR_{50}: 9.8 g a.i./ha NOEC (reproduction): <2.2 g a.i./ha	
Birds					
Bobwhite quail		Acute	spiromesifen	LD_{50} > 2000 mg a.i./kg bw NOEL < 500 mg a.i./kg BW (diarrhea)	Practically non-toxic
		Dietary	spiromesifen	LC_{50} > 4767 mg a.i./kg diet NOEL : 4767 mg a.i./kg diet	At most slightly toxic based on measured concentration
		Reproduction	spiromesifen	NOEC: 75 mg/kg feed (cracked eggs)	No classification
Mallard duck		Dietary	spiromesifen	LC_{50} > 5000 mg a.i./kg diet NOEC < 5000 mg a.i./kg diet	Practically non-toxic
		Reproduction	spiromesifen	NOEC: 229 mg a.i./kg diet (female and male body weight) NOEC: 229 mg a.i./kg diet (reproduction)	

Organism	Exposure	Test substance	End point value	Degree of toxicity[a]
Mammals				
Rat	Acute oral	spiromesifen	LD_{50} >2000 ppm NOAEL: 2000 ppm	Not toxic
	Dietary (28 d)	spiromesifen	NOAEL: 100 ppm (liver, spleen, kidney, cholesterol effects)	No classification
	Dietary (90 d)	spiromesifen	NOAEL: 100 ppm (thyroid, kidney and cholesterol effects)	No classification
	Reproduction (2 generation)	spiromesifen	NOAEL: 120 ppm (F_1 and F_2 bw, thymus)	No classification
Mouse	Dietary (90 d)	spiromesifen	NOAEL: 20 ppm (adrenal, cholesterol effects) female 80 ppm (adrenal, cholesterol effects) male	No classification
Vascular plants				
Vascular plant (Tier II)	Seedling emergence	EUP (Forbid 240 SC; 23% a.i.)	Based on dry weight for ryegrass: EC_{25}: **27 g a.i./ha** Based on phytotoxicity: EC_{25}: 57 g a.i./ha Based on survival: EC_{25}: 228 g a.i./ha	No classification
	Vegetative vigour	EUP (Forbid 240 SC; 23% a.i.)	Based on dry weight for turnip: EC_{25}: 180 g a.i./ha	No classification
Aquatic organisms				
Freshwater species (limit of solubility: 120 µg a.i./L)				
Daphnia magna	48 hr acute	spiromesifen	LC_{50} > 92.3 µg a.i./L NOEC: 92.3 µg a.i./L	Very highly toxic
		EUP (Forbid 240 SC; 23% a.i.)	EC_{50}: 17.8 mg a.i./L NOEC: 0.083 mg a.i./L (impaired mobility)	Slightly toxic
		transformation product (BSN enol)	LC_{50} > 101 mg TP/L NOEC: 101 mg TP/L	Practically non-toxic
	21 d chronic	spiromesifen	NOEC: 0.25 µg a.i./L (reproduction)	No classification

	24 d chronic	EUP (Forbid 240 SC; 23% a.i.)	NOEC: 1.7 µg a.i./L (mortality and reproduction)	No classification
	21 d chronic	transformation product (BSN enol)	NOEC: 186 µg TP/L (mortality and reproduction)	No classification
	chronic (51 d) population effects	EUP (Forbid 240 SC; 23% a.i.)	EAC: 0.56 µg a.i./L (full recovery)	No classification
Rainbow trout	96 hr acute	spiromesifen	LC_{50}: 16.8 µg a.i./L NOEC: 7.25 µg a.i./L	Very highly toxic
		EUP (Forbid 240 SC; 23% a.i.)	LC_{50}: 72.7 µg a.i./L NOEC: < 7.9 µg a.i./L (behavioural)	Very highly toxic
		transformation product (BSN enol)	LC_{50}: > 102 mg TP/L NOEC: 101 mg TP/L	Practically non-toxic
	96 d chronic	spiromesifen	NOEC: 4.73 µg a.i./L (swim up and length) NOEC: 7.84 µg a.i./L (time to hatch)	No classification
	28 d chronic	transformation product (BSN enol)	NOEC: 9.5 mg TP/L	No classification
Fathead minnow	96 hr acute	spiromesifen	LC_{50} > 40.1 µg a.i./L NOEC: 26.9 µg a.i./L (mortality)	Very highly toxic
	260 d chronic	spiromesifen	NOEC: 1.5 µg a.i./L (hatching)	No classification
Bluegill sunfish	96 h acute	spiromesifen	LC_{50} > 33.7 µg a.i./L NOEC: 13.9 µg a.i./L (mortality)	Very highly toxic
		EUP (Forbid 240 SC; 23% a.i.)	LC_{50}: 56.75 µg a.i./L NOEC: < 7.56 µg a.i./L (behavioural)	Very highly toxic
Freshwater alga (green algae)	96 h acute	spiromesifen	NOEC (cell density): 4 µg a.i./L; EC50> 44.3 µg a.i./L	No classification
		transformation product (BSN enol)	NOEC: 3.13 µg TP/L EC_{50}: 9.8 µg TP/L (cell density)	No classification
Vascular plant	Dissolved - 7 d	spiromesifen	NOEC: 101.3 µg a.i./L EC_{50} >101.3 µg a.i./L (cell density)	No classification

Chironomid	Chronic	spiromesifen	NOEC: 0.032 mg a.i./L (emergence) NOEC: 0.1 mg a.i./L (development) EC_{50}: 0.069 mg a.i./L (emergence)	No classification
Marine species				
Crustacean (mysid)	96 hr acute	spiromesifen	LC_{50} >76 µg a.i./L NOEC: 76 µg a.i./L	Very highly toxic
	28 d chronic	spiromesifen	LC_{50} > 11 µg a.i./L NOEC: 11 µg a.i./L	No classification
Mollusk (eastern oyster)	96 hr acute	spiromesifen	EC_{50} > 26 µg a.i./L (shell growth) NOEC: 3.2 µg a.i./L	Very highly toxic
Sheepshead minnow	96 h acute	spiromesifen	LC_{50} > 46.3 µg a.i./L NOEC: 46.3 µg a.i./L	Very highly toxic

Atkins et al. (1981) for bees and US EPA classification for others, where applicable.

Table 9 Screening Level Risk Assessment on Non-Target Terrestrial Species

Organism	Study Type	Test Substance	Endpoint value	EEC	RQ[a]	Exceeds LOC?	Refined assessment (10 d foliar $T_{1/2}$)	Exceeds LOC?	Refined assessment (corn + potato rate)	Exceeds LOC?
Invertebrates										
Earthworm	Acute - 14 d	spiromesifen	NOEC: 1000 mg a.i./kg LC_{50} ÷2=500 mg a.i./kg	0.337 mg a.i./kg soil	0.0003 0.0006	no	Not applicable			
	Chronic	EUP (Forbid SC 240; 23% a.i.)	NOEL: 0.75 mg a.i./kg	0.337 mg a.i./kg soil	0.449	no				
Bee	Contact - 48 h	spiromesifen	NOEL: 200 µg a.i./bee (=224 kg a.i./ha)	0.7318 kg a.i./ha	0.003	no				
	Oral - 48 h	spiromesifen	NOEL: 166.1 µg a.i./bee (=251 kg a.i./ha)	0.7318 kg a.i./ha	0.003	no				
Bee	Contact - 48 h	EUP (Forbid SC 240; 23% a.i.)	NOEL: 200 µg a.i./bee (= 224 kg a.i./ha)	0.7318 kg a.i./ha	0.003	no				
	Oral - 48 h	Forbid SC 240; 23% a.i.	NOEL: 25 µg a.i./bee (= 28 kg a.i./ha)	0.7318 kg a.i./ha	0.026	no				
Rove beetle	contact	Forbid SC 240; 23% a.i.	LR_{50}:>0.896 kg a.i./ha NOEC (reproduction): 0.896 kg a.i./ha	0.7318 kg a.i./ha	0.82	no	Not applicable			

Organism	Study Type	Test Substance	Endpoint value	EEC	RQ[a]	Exceeds LOC?	Refined assessment (10 d foliar $T_{1/2}$)	Exceeds LOC?	Refined assessment (corn + potato rate)	Exceeds LOC?
Carabid beetle	contact	Forbid SC 240; 23% a.i.	LR_{50}: > 0.656 kg a.i./ha NOEC (mortality and pupae consumed): 0.656 kg a.i./ha	0.7318 kg a.i./ha	1.11	Yes	RQ = 0.84	No	Not applicable	
Ladybird beetle	contact	Forbid SC 240; 23% a.i.	LR_{50}: 0.0417 kg a.i./ha NOEC (reproduction): 0.011 kg a.i./ha NOEC (mortality): 0.023 kg a.i./ha	0.7318 kg a.i./ha	17.5	Yes	RQ = 13.3	Yes	RQ = 5.6	Yes
Green lacewing	contact	Forbid SC 240; 23% a.i.	LR_{50}: >0.865 kg a.i./ha NOEC (reproduction and mortality): 0.865 kg a.i./ha	0.7318 kg a.i./ha	0.85	No	Not applicable			

Organism	Study Type	Test Substance	Endpoint value	EEC	RQ[a]	Exceeds LOC?	Refined assessment (10 d foliar $T_{1/2}$)	Exceeds LOC?	Refined assessment (corn + potato rate)	Exceeds LOC?
Predaceous mite	contact	Forbid SC 240; 23% a.i.	LR_{50}: 0.0648 NOEC (reproduction): 0.050 kg a.i./ha NOEC (mortality): 0.024 kg a.i./ha	0.7318 kg a.i./ha	11.3	Yes	RQ= 8.6	Yes	RQ= 3.6	Yes
Aphid parasitoid	contact	Forbid SC 240; 23% a.i.	LR_{50}: 0.0098 NOEC (mortality): 0.0043 kg a.i./ha NOEC (fecundity): <0.0022 kg a.i./ha	0.7318 kg a.i./ha	74.7	Yes	RQ = 56.6	Yes	RQ = 23.7	Yes
Birds[b]										
Bobwhite quail	Acute oral	spiromesifen	NOEL < 500 mg a.i./kg BW (diarrhea)	8.52 mg a.i./kg bw	0.017	no	Not applicable			
	Dietary 5 d	spiromesifen	NOEL : 4767 mg a.i./kg diet	128.12 mg a.i./kg dw diet	0.03	no				
	Reproduc-tion	spiromesifen	NOEC: 75 mg/kg feed (parental and reproductive toxicity)	128.12 mg a.i./kg dw diet	1.7	yes	RQ = 1.29	yes	RQ = 0.54	no

Organism	Study Type	Test Substance	Endpoint value	EEC	RQ[a]	Exceeds LOC?	Refined assessment (10 d foliar $T_{1/2}$)	Exceeds LOC?	Refined assessment (corn + potato rate)	Exceeds LOC?
Mallard duck	Dietary 5 d	spiromesifen	NOEC: 5000 mg a.i./kg diet	24.75 mg a.i./kg dw diet	0.005	no	Not applicable			
	Reproduc-tion	spiromesifen	NOEC: 229 mg a.i./kg diet (reproduction)	24.75 mg a.i./kg dw diet	0.108	no				
Mammals[c]										
Rat	Acute oral	spiromesifen	LD50>2000 mg/kg bw NOAEL: 2000 mg/kg bw	922.95	0.46	no	Not applicable			
	Dietary (28 d)	spiromesifen	NOAEL: 100 mg/kg bw/d (liver, spleen, kidney, cholesterol effects)	369.18	3.7	yes	RQ = 2.8	yes	RQ = 1.17	yes
	Dietary (90 d)	spiromesifen	NOAEL: 100 mg/kg bw/d (thyroid, kidney and cholesterol effects)	369.18	3.69	yes	RQ = 2.8	yes	RQ = 1.17	yes
	Reproduc-tion	spiromesifen	F_1 offspring: 120 ppm	369.18	3.08	yes	RQ = 2.3	yes	RQ = 0.98	no
Mouse	Dietary (90 d)	spiromesifen	NOAEL: 80 mg/kg bw/d (adrenal, cholesterol effects)	366.96	4.59	yes	RQ = 3.48	yes	RQ = 1.46	yes

Organism	Study Type	Test Substance	Endpoint value	EEC	RQ[a]	Exceeds LOC?	Refined assessment (10 d foliar $T_{1/2}$)	Exceeds LOC?	Refined assessment (corn + potato rate)	Exceeds LOC?
Vascular plants										
Vascular plants*	Tier II (seedling emergence and vegetative vigour)	EUP (Forbid SC 240; 23% a.i.)	Based on dry weight for ryegrass: EC_{25}: 27 g a.i./ha	835.2 g a.i./ha	30.9	yes	Not applicable			
			Based on phytotoxicity (chlorosis & stunting) for ryegrass: EC_{25}: 57 g a.i./ha	835.2 g a.i./ha	14.6	yes				
		EUP (Forbid SC 240; 23% a.i.)	Based on dry weight for turnip: EC_{25}: 57 g a.i./ha	835.2 g a.i./ha	14.6	yes				

[a] Risk quotient = exposure / toxicity, trigger for a refined assessment is > 50 for bees, > 2 for other arthropods and > 1 for all other organisms.

[b] Calculated using daily food intake rate of 0.0159 kg/day and body weight of 0.239 kg from study data.

[c] Calculated using daily food intake rate of 0.015 kg/day and body weight of 0.006 kg from study data.

LOC: level of concern

* For terrestrial plants, ryegrass most sensitive species tested from 10 species of plants.

Highlighted rows indicate that the screening level risk quotient exceeds the trigger for a refined assessment.

Table 10 Screening Level Risk Assessment on Non-Target Aquatic Species

Organism	Exposure	Test substance	End point value (correction factor)	EEC[a]	RQ	Level of concern exceeded?
Freshwater species						
Daphnia magna	48 hr acute	spiromesifen	LC_{50} > 92.3 µg a.i./L (½ LC_{50}: 46.15 µg a.i./L)	81 µg a.i./ L	1.8	yes
		Forbid 240 SC; 23% a.i.	EC_{50}: 17.8 mg a.i./L (½ EC_{50}: 8.9 mg a.i./L)	0.081 mg a.i./L	0	no
		transformation product (BSN enol)	LC_{50} > 101 mg TP/L (½ LC_{50}: 50.5 mg TP/L)	0.081 mg a.i./L	0	no
	21 d chronic	spiromesifen	NOEC: 0.25 µg a.i./L (reproduction)	81 µg a.i./L	324	yes
	24 d chronic	Forbid 240 SC; 23% a.i.	NOEC: 1.7 µg a.i./L (mortality and reproduction)	81 µg a.i./L	47.6	yes
	21 d chronic	transformation product (BSN enol)	NOEC: 186 µg TP/L (mortality and reproduction)	81 µg a.i./L	0.435	no
	chronic population study	Forbid 240 SC; 23% a.i.	EAC (full recovery): 0.56 µg a.i./L	81 µg a.i./L	144.6	yes
Rainbow trout	96 hr acute	spiromesifen	LC_{50}: 16.8 µg a.i./L (1/10 LC_{50}: 1.68 µg a.i./L)	81 µg a.i./L	48.2	yes
		Forbid 240 SC; 23% a.i.	LC_{50}: 72.7 µg a.i./L (1/10 LC_{50}: 7.27 µg a.i./L)	81 µg a.i./L	11.1	yes
		transformation product (BSN enol)	LC_{50}: > 102 mg TP/L (1/10 LC_{50}: 10.2 mg TP/L)	0.081 mg a.i./L	0	no
	96 d chronic	spiromesifen	NOEC: 4.73 µg a.i./L (swim up and length)	81 µg a.i./L	17.1	yes
	28 d chronic	transformation product (BSN enol)	NOEC: 9.5 mg TP/L	0.081 mg a.i./L	0	no
Fathead minnow	96 hr acute	spiromesifen	LC50> 40.1 µg a.i./L (1/10 LC_{50}: 4.0 µg a.i./L)	81 µg a.i./L	20.25	yes
	260 d chronic	spiromesifen	NOEC: 1.5 µg a.i./L (hatching)	81 µg a.i./L	54	yes

Organism	Exposure	Test substance	End point value (correction factor)	EEC[a]	RQ	Level of concern exceeded?
Bluegill sunfish	96 h acute	spiromesifen	LC50> 33.7 µg a.i./L (1/10 LC_{50}: 3.37 µg a.i./L)	81 µg a.i./L	24	yes
		Forbid 240 SC; 23% a.i.	LC_{50}: 56.75 µg a.i./L (1/10 LC_{50}: 5.68 µg a.i./L)	81 µg a.i./L	14.26	yes
			sublethal: EC_{50}: 7.56 µg a.i./L (loss of equilibrium)	81 µg a.i./L	10.7	yes
Freshwater alga (green algae)	96 h acute	spiromesifen	EC50> 44.3 µg a.i./L (½ EC_{50}: 22.2 µg a.i./L)	81 µg a.i./L	3.6	yes
		transformation product (BSN enol)	EC_{50}: 9.8 µg TP/L (cell density) (½ EC_{50}: 4.9 µg TP/L)	53.6 µg a.i./L [c]	10.9	yes
Vascular plant	Dissolved - 7 d	spiromesifen	EC50>101.3 µg a.i./L (cell density) (½ EC_{50}: 50.7 µg a.i./L)	81 µg a.i./L	1.6	yes
Chironomid	Chronic	spiromesifen	NOEC: 0.032 mg a.i./L (emergence)	0.081 mg a.i./L	2.5	yes
Amphibians [b]						
Amphibians	Acute (based on acute fish studies)	spiromesifen	LC_{50} for rainbow trout (most sensitive species): (1/10 the LC_{50}: 1.68 µg a.i./L)	430 µg a.i./L	256	yes
	Acute (based on acute fish studies)	TP - BSN 2060-enol	LC_{50} for rainbow trout (most sensitive species): (1/10 the LC_{50}: 10.2 mg a.i./L)	0.43 mg a.i./L	0.04	no
	Chronic (based on early life stage fish study)	spiromesifen	NOEC for ELS study with fathead minnow: 1.5 µg a.i./L	430 µg a.i./L	287	yes
Marine species						
Crustacean (mysid)	96 hr acute	spiromesifen	LC50> 76 µg a.i./L (½ LC50> 38 µg a.i./L)	81 µg a.i./L	2.1	yes
	28 d chronic	spiromesifen	NOEC: 11 µg a.i./L	81 µg a.i./L	7.4	yes

Organism	Exposure	Test substance	End point value (correction factor)	EEC[a]	RQ	Level of concern exceeded?
Mollusk (eastern oyster)	96 hr acute	spiromesifen	EC50> 26 µg a.i./L (shell growth) (½ EC_{50}: 13 µg a.i./L)	81 µg a.i./L	6.2	yes
Sheepshead minnow	96 h acute	spiromesifen	LC_{50}: 46.3 µg a.i./L (1/10 LC_{50}: 4.63 µg a.i./L)	81 µg a.i./L	17.5	yes

[a] 15 cm depth used for EEC in water calculation

[b] 80 cm depth used for EEC in water calculation

[c] The EEC was calculated by using the parent rate x 90% adjusted for the molar ratio.

Highlighted rows indicate that the screening level risk quotient exceeds the trigger for a refined assessment.
RQ = EEC in a 80-cm deep water body / (EC_{50} ÷ 2 or LC_{50} ÷ 2); for a chronic exposure: RQ = EEC in a 80-cm deep water body / NOEC.

Table 11 Refined Risk Assessment on Non-Target Species

Organism (exposure)	Test substance	Endpoint (mg a.i./L)	EEC based on 11% drift for ground boom sprayer application[a]	RQ	Level of concern exceeded?	Factors	Used in refined risk assessment?
Terrestrial							
Terrestrial plants	Forbid SC 240; 23% a.i.	Based on dry weight for ryegrass: EC_{25}: 27 g a.i./ha	91.9 g a.i./ha	3.4	Yes	Drift may occur to non-target plants.	Yes **(ryegrass: EC_{25}: 27 g a.i./ha)**
Ladybird beetle	Forbid SC 240; 23% a.i.	LR_{50}: 0.0417 kg a.i./ha	0.061 kg a.i./ha	1.46	Yes	Drift may occur to predator and parasites.	Yes
Predaceous mite	Forbid SC 240; 23% a.i.	LR_{50}: 0.0648 kg a.i./ha	0.061 kg a.i./ha	0.94	No	not applicable	not applicable
Aphid parasitoid	Forbid SC 240; 23% a.i.	LR_{50}: 0.0098 kg a.i./ha	0.061 kg a.i./ha	6.22	Yes	Drift may occur to predator and parasites.	Yes (LR_{50}: 0.0098 kg a.i./ha)
Bobwhite quail	spiromesifen	NOEC: 75 mg/kg feed (parental and reproductive toxicity)	14.1 mg a.i./kg dw diet	0.18	No	not applicable	not applicable
Rat	spiromesifen	NOAEL: 100 mg/kg bw/d (liver, spleen, kidney, cholesterol effects)	40.61 mg a.i./kg dw diet	0.41	No	not applicable	not applicable
	spiromesifen	NOAEL: 100 mg/kg bw/d (thyroid, kidney and cholesterol effects)	40.61 mg a.i./kg dw diet	0.41	No	not applicable	not applicable
Mouse	spiromesifen	NOAEL: 80 mg/kg bw/d (adrenal, cholesterol effects)	40.37 mg a.i./kg dw diet	0.5	No	not applicable	not applicable

Organism (exposure)	Test substance	Endpoint (mg a.i./L)	EEC based on 11% drift for ground boom sprayer application[a]	RQ	Level of concern exceeded?	Factors	Used in refined risk assessment?
Aquatic							
Daphnid	spiromesifen	LC_{50} > 92.3 µg a.i./L (½ LC_{50}: 46.15 µg a.i./L)	8.91 µg/L	0.19	No	not applicable	not applicable
	spiromesifen	NOEC: 0.25 µg a.i./L (reproduction)	8.91 µg a.i./L	35.6	Yes	Spiromesifen has limited solubility, a short half life in water and partitions to sediment, chronic exposure is not expected, even with a maximum of three applications per year. Therefore, a flow through study is not representative of the chemical.	No (0.25 µg a.i./L (reproduction))
	Forbid SC 240; 23% a.i.	NOEC: 1.7 µg a.i./L (mortality and reproduction)	8.91 µg a.i./L	5.24	Yes	This study design actually simulated a realistic environmental application scenario, and effects on mortality and reproduction were observed at low concentrations.	Yes (NOEC: 1.7 µg a.i./L)
	Forbid SC 240; 23% a.i.	EAC: 0.56 µg a.i./L	8.91 µg a.i./L	15.9	Yes	This study design actually simulated a realistic environmental application scenario.	**EAC: 0.56 µg a.i./L)**

Organism (exposure)	Test substance	Endpoint (mg a.i./L)	EEC based on 11% drift for ground boom sprayer application[a]	RQ	Level of concern exceeded?	Factors	Used in refined risk assessment?
Rainbow trout	spiromesifen	LC_{50}: 16.8 µg a.i./L (1/10 LC_{50}: 1.68 µg a.i./L)	8.91 µg a.i./L	5.3	Yes	This study design simulated acute exposure, and effects on mortality were observed at low concentrations.	Yes (1/10 LC_{50}: 1.68 µg a.i./L)
	Forbid SC 240; 23% a.i.	LC_{50}: 72.7 µg a.i./L (1/10 LC_{50}: 7.27 µg a.i./L)	8.91 µg a.i./L	1.22	Yes	This study design simulated acute exposure, and effects on mortality were observed at low concentrations.	Yes (1/10 LC_{50}: 7.27 µg a.i./L)
	spiromesifen	NOEC: 4.73 µg a.i./L (swim up and length)	8.91 µg a.i./L	1.88	Yes	Since spiromesifen has limited solubility, a short half life in water and partitions to sediment, chronic exposure is not expected, even with a maximum of three applications per year. Therefore, a flow through study is not representative of the chemical.	No (NOEC: 4.73 µg a.i./L (swim up and length))

Organism (exposure)	Test substance	Endpoint (mg a.i./L)	EEC based on 11% drift for ground boom sprayer application[a]	RQ	Level of concern exceeded?	Factors	Used in refined risk assessment?
Fathead minnow	spiromesifen	LC_{50} > 40.1 µg a.i./L (1/10 LC_{50}: 4.01 µg a.i./L)	8.91 µg a.i./L	2.22	Yes	This study is short term.	Yes (1/10 LC_{50}: 4.01 µg a.i./L))
	spiromesifen	NOEC: 1.5 µg a.i./L (hatching)	8.91 µg a.i./L	5.94	Yes	Since spiromesifen has limited solubility, a short half life in water and partitions to sediment, chronic exposure is not expected, even with a maximum of three applications per year. Therefore, a flow through study is not representative of the chemical.	No (NOEC: 1.5 µg a.i./L (hatching))
Bluegill sunfish	spiromesifen	LC_{50} > 33.7 µg a.i./L (1/10 LC_{50}: 3.37 µg a.i./L)	8.91 µg a.i./L	2.64	Yes	This study is short term.	Yes (1/10 LC_{50}: 3.37 µg a.i./L)
	Forbid SC 240; 23% a.i.	LC_{50}: 56.75 µg a.i./L (1/10 LC_{50}: 5.68 µg a.i./L)	8.91 µg a.i./L	1.57	Yes	This study is short term.	Yes (1/10 LC_{50}: 5.68 µg a.i./L)
		EC100%: 7.56 µg a.i./L	8.91 µg a.i./L	1.18	Yes	This study is short term.	Yes EC100%: 7.56 µg a.i./L

Organism (exposure)	Test substance	Endpoint (mg a.i./L)	EEC based on 11% drift for ground boom sprayer application[a]	RQ	Level of concern exceeded?	Factors	Used in refined risk assessment?
Freshwater alga	spiromesifen	EC_{50} > 44.3 µg a.i./L (½ EC_{50}: 22.2 µg a.i./L)	8.91 µg a.i./L	0.4	No	not applicable	not applicable
	transformation product (BSN enol)	EC_{50}: 9.8 µg TP/L (cell density) (½ EC_{50}: 4.9 µg TP/L)	5.9 µg TP/L	1.2	Yes	This study design simulated acute exposure, and effects on mortality were observed at very low concentrations. In addition, there is no limit on the solubility of BSN 2060-enol, and it is persistent in water.	Yes (½ EC_{50}: 4.9 µg TP/L)
Vascular plant	spiromesifen	EC_{50} >101.3 µg a.i./L (cell density) (½ EC_{50}: 50.7 µg a.i./L)	8.91 µg a.i./L	0.18	No	not applicable	not applicable
Chironomid	spiromesifen	NOEC: 0.032 mg a.i./L (emergence)	0.00891 mg a.i./L	0.28	No	not applicable	not applicable

Organism (exposure)	Test substance	Endpoint (mg a.i./L)	EEC based on 11% drift for ground boom sprayer application[a]	RQ	Level of concern exceeded?	Factors	Used in refined risk assessment?
Amphibians	spiromesifen	LC_{50} for rainbow trout (most sensitive species): (1/10 the LC_{50}: 1.68 µg a.i./L)	47.3 µg/L	28.2	Yes	This study design simulated acute exposure.	**Yes (1/10 LC_{50}: 1.68 µg a.i./L)**
	spiromesifen	NOEC for ELS study with fathead minnow: 1.5 µg a.i./L	47.3 µg/L	31.5	Yes	Since spiromesifen has limited solubility, a short half life in water and partitions to sediment, chronic exposure is not expected, even with a maximum of three applications per year. Therefore, a flow through study is not representative of the chemical. In addition, tadpoles are expected to be exposed until adulthood, at which time they will be both on land and in water, and have less aquatic exposure.	No (NOEC for ELS study with fathead minnow: 1.5 µg a.i./L)
Mysid	spiromesifen	LC_{50} > 76 µg a.i./L (½ LC_{50}: 38 µg a.i./L)	8.91 µg a.i./L	0.23	No	not applicable	not applicable
	spiromesifen	NOEC: 11 µg a.i./L	8.91 µg a.i./L	0.81	No	not applicable	not applicable

Organism (exposure)	Test substance	Endpoint (mg a.i./L)	EEC based on 11% drift for ground boom sprayer application[a]	RQ	Level of concern exceeded?	Factors	Used in refined risk assessment?
Mollusc	spiromesifen	EC_{50} > 26 µg a.i./L (shell growth) (½ EC_{50}: 13 µg a.i./L)	8.91 µg a.i./L	0.69	No	not applicable	not applicable
Sheepshead minnow	spiromesifen	LC_{50}: 46.3 µg a.i./L (1/10 LC_{50}: 4.63 µg a.i./L)	8.91 µg a.i./L	1.92	Yes	This study is short term, and the most sensitive marine species.	**Yes (1/10 LC_{50}: 4.63 µg a.i./L)**

Drift estimate EAD model for ground application based on data of Wolf and Caldwell (2001).
bolded values will have buffer zones calculated.

Table 12 Risk Assessment on Aquatic Organisms from Surface Runoff

Organism (exposure)	Test substance	Endpoint (µg a.i./L)	EEC 90th percentile concentration (µg a.i./L) (time-frame and scenario)[a]	RQ	Level of Concern
Daphnia (acute)	spiromesifen	½ LC_{50}: 46.15	0.498	0.011	Not exceeded
Daphnia (chronic)	spiromesifen	NOEC: 0.25	0.175	0.7	Not exceeded
	Forbid 240 SC	NOEC: 1.7	0.175	0.103	Not exceeded
Daphnia (chronic)	Forbid 240 SC	EAC: 0.56	0.107	0.19	Not exceeded
Rainbow trout (acute)	spiromesifen	1/10 LC_{50}: 1.68	0.498	0.296	Not exceeded
	Forbid 240 SC	1/10 LC_{50}: 7.27	0.498	0.069	Not exceeded
Rainbow trout (chronic	spiromesifen	NOEC: 4.73	0.107	0.023	Not exceeded
Fathead minnow (acute)	spiromesifen	1/10 LC_{50}: 4.01	0.498	0.124	Not exceeded
Fathead minnow (chronic)	spiromesifen	NOEC: 1.5	0.034	0.023	Not exceeded
Bluegill sunfish (acute)	spiromesifen	1/10 LC_{50}: 3.37	0.498	0.148	Not exceeded

Organism (exposure)	Test substance	Endpoint (µg a.i./L)	EEC 90th percentile concentration (µg a.i./L) (time-frame and scenario)[a]	RQ	Level of Concern
Bluegill sunfish (acute)	Forbid 240 SC	1/10 LC_{50}: 5.68	0.498	0.088	Not exceeded
		EC100: 7.56	0.498	0.066	Not exceeded
Green alga (acute)	spiromesifen	½ EC_{50}: 22.2	0.498	0.022	Not exceeded
	BSN 2060-enol	½ EC_{50}: 4.9	1084	221	Exceeded
Lemna	spiromesifen	½ EC_{50}: 50.7	0.498	0.01	Not exceeded
Chironomid (chronic)	spiromesifen	NOEC: 32	0.052	0	Not exceeded
Amphibians (acute)	spiromesifen	1/10 LC_{50}: 1.68	0.498	0.296	Not exceeded
Amphibians (chronic)	spiromesifen	NOEC: 1.5	0.09	0.06	Not exceeded
Mysid (acute)	spiromesifen	½ LC_{50}: 38	0.498	0.013	Not exceeded
Mysid (chronic)	spiromesifen	NOEC: 11	0.175	0.016	Not exceeded
Mollusc (acute)	spiromesifen	½ EC_{50}: 13	0.498	0.038	Not exceeded
Sheepshead minnow (acute)	spiromesifen	½ LC_{50}: 4.63	0.498	0.108	Not exceeded

a = acute EEC (96 hr); chronic daphnid and mysid EEC (21 d); chronic daphnid population study EEC (60 d); chronic fathead minnow EEC (yearly) benthic EEC for chironomid; chronic amphibian EEC (90 d)

Table 13 Refined risk quotients for aquatic species determined for runoff of BSN 2060-enol

Organism (exposure)	Test substance	Refinement scenario	Endpoint (µg a.i./L)	EEC 90th percentile concentration (µg a.i./L) (time-frame and scenario)	RQ	Risk
Green alga (acute)	BSN 2060-enol	Corn Quebec	½ EC_{50}: 4.9	57.796	11.8	Exceeded
Green alga (acute)	BSN 2060-enol	Corn Ontario	½ EC_{50}: 4.9	37.93	7.74	Exceeded

Table 14 Alternative Insecticides for Mite and Whitefly Control in the Labelled Crops

Active Ingredient	Insecticide Resistance Management Group	Registered Crops	
		Whiteflies	Mites
Bendiocarb	1A	Interior plant scapes; greenhouse ornamentals	
Carbaryl & pirimicarb	1A	Roses and flowers	
Acephate	1B	Greenhouse ornamentals	
Diazinon	1B		Outdoor ornamentals; strawberries; cantaloupe; cucumber; muskmelon; squash; watermelon
Malathion	1B	Outdoor ornamentals (flowers, shrubs, trees); vegetables; fruits; Greenhouse flowers; Greenhouse lettuce	Eggplant; field and greenhouse lettuce; endive; outdoor and greenhouse ornamentals; potato; tomato; celery; garlic; leek; onion; pea; shallot; salsify; cucumber; melon; pumpkin; squash
Chlorpyrifos	1B	Greenhouse ornamentals; nurseries; industrial sites;	Industrial sites; nurseries; greenhouse ornamentals
Dichlorvos	1B	Greenhouse ornamentals	
Dimethoate	1B	Outdoor flowering plants	Outdoor ornamentals; strawberries
Naled	1B	Greenhouse tomatoes, cucumbers, roses and cut flowers	greenhouse tomatoes and cucumber; greenhouse roses and flowers
Endosulfan	2A	Greenhouse tomato and cucumber; greenhouse and outdoor ornamental	

Active Ingredient	Insecticide Resistance Management Group	Registered Crops	
		Whiteflies	Mites
d-Phenothrin & tetramethrin	3	houseplants; outdoor ornamentals;	
Permethrin	3	tomato; greenhouse (indoor) ornamentals, tomatoes & cucumbers; potatoes; outdoor roses, flowers and ornamentals;	
Pyrethrin and piperonyl butoxide	3 and 27A	outdoor and indoor ornamentals; Broccoli; Brussels Sprouts; Cabbage; Cauliflower; Celery; Collards; Corn; Cucumbers; Eggplant; Kale; Lettuce; Melon; Mustard Greens; Peppers; Potatoes; Radishes; Spinach; squash; Swiss chard; Tomatoes; Turnips; Houseplants;	
Acetampirid	4A	Flowers & ornamental plants; Brassica (cole) crops; Field tomato; Ornamental and flowering plants grown outdoors and in greenhouses, shadehouses and lathhouses;	
Imidacloprid	4A	Greenhouse ornamentals; Peppers	
Abamectin	6		Greenhouse ornamentals; greenhouse peppers, cucumber and tomato; strawberries
(S)-Kinoprene	7A	Greenhouse ornamentals	
Pymetrozine	9A	Greenhouse ornamentals	
Clofentezine	10A		Outdoor nursery stock; strawberries
Fenbutatin oxide	12B		Greenhouse cucumber and tomato; greenhouse and outdoor ornamentals
Pyridaben	21	Greenhouse ornamentals	Greenhouse and outdoor ornamentals; greenhouse tomato, cucumber and pepper; strawberries
Bifenazate	25		Indoor ornamentals; greenhouse tomato, cucumber and pepper
Dicofol	Unclassified		Strawberries; melons; pumpkin; squash; tomato; pepper
Mineral oil	Unclassified	Woody outdoor ornamentals	Wood ornamentals
Parafinic oil	Unclassified		Ornamental plants

Active Ingredient	Insecticide Resistance Management Group	Registered Crops	
		Whiteflies	Mites
Soap	Unclassified	Greenhouse plantings; Greenhouse tomatoes, peppers and cucumbers; Vegetables; Outdoor ornamentals; Shrubs; Trees; Houseplants	Ornamentals; vegetables; fruits; shrubs; trees; greenhouse and interior plantings
Sulphur	Unclassified		Ornamentals

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

Applicant-proposed Label Claims	Accepted Label Claims	Unsupported Label Claims and Comments
Pests of Fruiting Vegetables: Broad mite, potato/tomato psyllid, two-spotted spider mite, whiteflies (including silverleaf, sweetpotato and greenhouse)	Broad mite, two-spotted spider mite, whiteflies (including silverleaf, sweetpotato and greenhouse)	Potato/tomato psyllid
Pests of Tuberous and Corm Vegetables: Potato/tomato psyllid, two-spotted spider mite, whiteflies (including silverleaf, sweetpotato and greenhouse)	Two-spotted spider mite, whiteflies (including silverleaf, sweetpotato and greenhouse)	Potato/tomato psyllid
Pests of Strawberries: Two-spotted spider mite, whiteflies (including silverleaf, sweetpotato and greenhouse), cyclamen mite	Two-spotted spider mite, whiteflies (including silverleaf, sweetpotato and greenhouse)	Cyclamen mite
Pests of outdoor ornamentals: Spider mites (including two-spotted spider mite, southern red mite, maple spider mite, spruce spider mite, honeylocust spider mite, Euonymus mite, boxwood spider mite, tumid mite and Lewis mite), False spider mites, Rust and blister mites (family Eriophyidae), Tarsonemid mites (including broad mites and cyclamen mite), Whiteflies (including silverleaf, greenhouse and sweet potato whitefly)	Two-spotted spider mite and whiteflies (including silverleaf, greenhouse and sweet potato whitefly)	Southern red mite, maple spider mite, spruce spider mite, honeylocust spider mite, Euonymus mite, boxwood spider mite, tumid mite, Lewis mite, False spider mites, Rust and blister mites (family Eriophyidae), Tarsonemid mites (including broad mites and cyclamen mite)
Application methods: Ground, aerial and chemigation	Ground and aerial	Chemigation

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

Twenty-two of the specified Canadian MRLs are the same as those in the U.S. In 7 cases, the MRL differs from the tolerance established in the U.S.
www.access.gpo.gov/nara/cfr/waisidx_04/40cfr180_04.html

Table 1 Differences Between Canadian MRLs and Other Jurisdictions

Commodity	Canada (ppm)	U.S. (ppm)	Codex* (ppm)
Corn, field, grain	0.02	0.02	None
Strawberry	2	2	
Tomato, paste	0.6	0.6	
Vegetable, brassica, head and stem, subgroup 5A	2	2	
Vegetable, brassica, leafy greens, subgroup 5B	12	12	
Vegetable, cucurbit, group 9, except cucumber	0.1	0.1	
Cucumber	0.2	0.1	
Vegetable, fruiting, group 8, except cherry tomato	0.45	0.45	
Cherry tomato	0.6	0.45	
Vegetable, leafy greens, subgroup 4A	12	12	
Vegetable, tuberous and corm, subgroup 1C	0.02	0.02	
Barley, grain	0.03	0.03	
Wheat, grain	0.03	0.03	
Beet, sugar, roots	0.03	0.03	
Beet, sugar, tops	0.2	0.2	
Cattle, fat	0.05	0.05	
Cattle, meat byproducts	0.05	0.05	
Goat, fat	0.05	0.05	
Goat, meat byproducts	0.05	0.05	

Commodity	Canada (ppm)	U.S. (ppm)	Codex* (ppm)
Horse, fat	0.05	0.05	
Horse, meat byproducts	0.05	0.05	
Sheep, fat	0.05	0.05	
Sheep, meat byproducts	0.05	0.05	
Milk, fat	0.1	0.1	
Milk	0.005	None	
Cattle, meat	0.01	None	
Goat, meat	0.01	None	
Horse, meat	0.01	None	
Sheep, meat	0.01	None	

* Codex is an international organization under the auspices of the United Nations that develops international food standards, including MRLs.

MRLs may vary from one country to another for a number of reasons, including differences in pesticide use patterns and the locations of the field crop trials used to generate residue chemistry data. For animal commodities, differences in MRLs can be due to different livestock feed items and practices.

Under the North American Free Trade Agreement (NAFTA), Canada, the United States and Mexico are committed to resolving MRL discrepancies to the broadest extent possible. Harmonization will standardize the protection of human health across North America and promote the free trade of safe food products. Until harmonization is achieved, the Canadian MRLs specified in this document are necessary. The differences in MRLs outlined above are not expected to impact businesses negatively or adversely affect international competitiveness of Canadian firms or to negatively affect any regions of Canada.

Appendix III Crop Groups: Numbers and Definitions

Crop Group Number	Name of the Crop Group	Commodity
1C	Tuberous and Corm Vegetables	arracacha
1C	Tuberous and Corm Vegetables	arrowroot
1C	Tuberous and Corm Vegetables	cassava roots
1C	Tuberous and Corm Vegetables	chayote roots
1C	Tuberous and Corm Vegetables	Chinese artichokes
1C	Tuberous and Corm Vegetables	chufa
1C	Tuberous and Corm Vegetables	edible canna
1C	Tuberous and Corm Vegetables	ginger roots
1C	Tuberous and Corm Vegetables	Jerusalem artichokes
1C	Tuberous and Corm Vegetables	lerens
1C	Tuberous and Corm Vegetables	potatoes
1C	Tuberous and Corm Vegetables	sweet potato roots
1C	Tuberous and Corm Vegetables	tanier corms
1C	Tuberous and Corm Vegetables	taro corms
1C	Tuberous and Corm Vegetables	true yam tubers
1C	Tuberous and Corm Vegetables	turmeric roots
1C	Tuberous and Corm Vegetables	yam bean roots
4A	Leafy Greens	amaranth
4A	Leafy Greens	arugula
4A	Leafy Greens	corn salad
4A	Leafy Greens	dandelion leaves
4A	Leafy Greens	dock
4A	Leafy Greens	edible leaved chrysanthemum
4A	Leafy Greens	endives
4A	Leafy Greens	fresh chervil leaves
4A	Leafy Greens	garden cress
4A	Leafy Greens	garden purslane
4A	Leafy Greens	garland chrysanthemum
4A	Leafy Greens	head lettuce
4A	Leafy Greens	leaf lettuce
4A	Leafy Greens	New Zealand spinach
4A	Leafy Greens	orach leaves
4A	Leafy Greens	parsley leaves
4A	Leafy Greens	radicchio
4A	Leafy Greens	spinach
4A	Leafy Greens	upland cress
4A	Leafy Greens	vine spinach
4A	Leafy Greens	winter purslane
5A	Head and Stem Brassica	broccoli
5A	Head and Stem Brassica	Brussels sprouts
5A	Head and Stem Brassica	cabbages
5A	Head and Stem Brassica	cauliflower
5A	Head and Stem Brassica	Chinese broccoli
5A	Head and Stem Brassica	Chinese mustard cabbage
5A	Head and Stem Brassica	kohlrabi
5A	Head and Stem Brassica	Napa Chinese cabbage

Crop Group Number	Name of the Crop Group	Commodity
5B	Leafy Brassica Greens	bok choy Chinese cabbage
5B	Leafy Brassica Greens	broccoli raab
5B	Leafy Brassica Greens	collards
5B	Leafy Brassica Greens	kale
5B	Leafy Brassica Greens	mustard greens
5B	Leafy Brassica Greens	mustard spinach
5B	Leafy Brassica Greens	rape greens
8	Fruiting Vegetable	bell peppers
8	Fruiting Vegetable	eggplants
8	Fruiting Vegetable	groundcherries
8	Fruiting Vegetable	non-bell peppers
8	Fruiting Vegetable	pepinos
8	Fruiting Vegetable	pepper hybrids
8	Fruiting Vegetable	tomatillos
8	Fruiting Vegetable	tomatoes
9	Cucurbit Vegetable	balsam apples
9	Cucurbit Vegetable	balsam pears
9	Cucurbit Vegetable	cantaloupes
9	Cucurbit Vegetable	chayote fruit
9	Cucurbit Vegetable	Chinese cucumbers
9	Cucurbit Vegetable	Chinese waxgourds
9	Cucurbit Vegetable	citron melons
9	Cucurbit Vegetable	cucumbers
9	Cucurbit Vegetable	edible gourds (other than those listed in this item)
9	Cucurbit Vegetable	muskmelons (other than those listed in this item)
9	Cucurbit Vegetable	pumpkins
9	Cucurbit Vegetable	summer squash
9	Cucurbit Vegetable	watermelons
9	Cucurbit Vegetable	West Indian gherkins
9	Cucurbit Vegetable	winter squash

List of References

A. LIST OF STUDIES/INFORMATION SUBMITTED BY REGISTRANT

1.0 Chemistry Assessment

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3.0 Impact on Human and Animal Health

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1296172 2002, BSN 2060 240 SC - magnitude of the residue on mustard greens, Bayer Corporation, Stilwell, KS, USA, 200172, MRID: 45819426, DACO: 7.4.1

1296173 2002, BSN 2060 240 SC - magnitude of the residue on strawberries, Bayer Corporation, Stilwell, KS, USA, 110315, MRID: 45819411, DACO: 7.4.1

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1296179 2002, BSN 2060 240 SC - magnitude of the residue on corn, Bayer Corporation, Stilwell, KS, USA, 200178, MRID: 45819501, DACO: 7.4.1

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1296188 2001, Determination of residues of BSN 2060 on pepper after spray application of BSN 2060 240 SC in the greenhouse in the Netherlands, Bayer AG, Leverkusen, Germany, RA-2021/00, DACO: 7.4.1

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1296285 2002, BSN 2060 240 SC - magnitude of the residue in alfalfa (rotational crop tolerance), Bayer CropScience, Stilwell, KS, USA, 200112, MRID: 45819424, DACO: 7.4.4

1296288 2002, BSN 2060 240 SC - magnitude of the residue in sugar beets (rotational crop tolerance), Bayer Corporation, Stilwell, KS, USA, 200161, MRID: 45819428, DACO: 7.4.4

1296292 2002, BSN 2060 240 SC - magnitude of the residue in wheat (rotational crop tolerance), Bayer Corporation, Stilwell, KS, USA, 200185, MRID: 45819503, DACO: 7.4.4

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1296277 2001, Determination of residues of BSN 2060 on tomato (fruit; fruit washed; juice; preserve; fruit peeled; washings; pomace wet; peeling water w. peel; raw juice) after spray application of BSN 2060 240 SC in the greenhouse in Germany and Belgium,

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1296279 2002, BSN 2060 240 SC - magnitude of the residue in corn processed commodities (request for waiver of the study for the magnitude of the residue in corn aspirated grain fractions and processed commodities), Bayer Corporation, Stilwell, KS, USA, 200180, MR

1296280 2002, BSN 2060 240 SC - magnitude of the residue in wheat processed commodities and request for waiver of the study for the magnitude of the residue in wheat aspirated grain fractions from wheat grown as a rotational crop, Bayer Corporation, Stilwell, KS,

1296284	2002, BSN 2060 240 SC - Magnitude of the residue on/in tomato processed commodities, Bayer Corporation, Stilwell, KS, USA, 110991, DACO: 7.4.5
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1296238	2002, BSN 2060 - A 28 - day dairy cattle feeding study, Bayer Corporation, Kansas City, MO, USA, 110318, MRID: 45819412, DACO: 7.4.6,7.5
1296273	2002, Storage stability of residues of BSN 2060 and BSN 2060-enol (BSN 0564) in/on matrices of plant origin during deep-fronzen storage over 24 months, Bayer CropScience AG, Monheim, Germany, MR-513/01, DACO: 7.3
1296283	2002, Request for waiver of poultry feeding study and residue analytical method for BSN 2060, Bayer Corporation, Stilwell, KS, USA, 200324, DACO: 7.5
1296246	2002, An exploratory study to determine the rate and route of eliminationof BSN 2060-phenyl-UL-14C when administered intravenously or dermally to male Rhesus monkeys, G200207, MRID: 45819828, DACO: 5.8
1296247	2002, A study to determine the dermal absorption of BSN 2060 in a SC 480 formulation when administered dermally to male Rhesus monkeys, G200208, DACO: 5.8

4.0 Impact on the Environment

PMRA Number	Title
1296624	2005, Hydrolysis of BSN 2060 in pH 4, 7, and 9 sterile aqueous buffer solutions at 25 and 50 centigrade degrees, Bayer Corporation, Stilwell, KS, USA, 109481-1, MRID: 45819734, DACO: 8.2.3.2
1296636	2001, Aerobic aquatic metabolism of [dihydrofuranone-3-14C]BSN 2060 in a Fresno, California, water and sediment system, Bayer Corporation, 110044, DACO: 8.2.3.5.4

1296637 2001, Anaerobic aquatic metabolism of [dihydrofuranone-3-14C]BSN 2060 in a Fresno, California, water and sediment system, Bayer Corporation, 110039, DACO: 8.2.3.5.6

1296642 2001, Aerobic aquatic metabolism of [dihydrofuranone-3-14C]BSN 2060 in a German water and sediment system, Bayer Corporation, 110045, MRID: 45819804, DACO: 8.2.3.5.4

1296643 2001, Aerobic degradation and metabolism of [phenyl-UL-14C]BSN 2060 in soil, Bayer AG, MR-361/00, DACO: 8.2.3.4.2

1296644 2001, Aerobic degradation and metabolism of [dihydrofuranone-3-14C]BSN 2060 in soils, Bayer AG, MR-229/01, DACO: 8.2.3.4.2

1296645 2001, Aerobic soil metabolism of [cyclopentyl-1-14C]BSN 2060 in Fresno, California soil, Bayer Corporation, 110450, DACO: 8.2.3.4.2

1296646 2001, Calculation of degradation rates of BSN 2060 and its metabolites BSN 2060-Enol and BSN 2060-4-carboxy based on aerobic soil degradation studies, Bayer AG, MR-501/01, DACO: 8.2.3.4.2

1296648 2001, Aqueous photolysis of [cyclopentyl-1-14C] BSN 2060-enol in pH 7 sterile buffer solution at 25 centigrade degrees, Bayer Corporation, 110596, MRID: 45819809, DACO: 8.2.3.3.2

1296650 2001, Soil photolysis of [dihydrofuranone-3-14C]BSN 2060, Bayer Corporation, 110028, MRID: 45819801, DACO: 8.2.3.3.1

1296686 1998, Adsorption/desorption of BSN 0546 (tetronic acid BSN 2060) on soils, IM1978, DACO: 8.2.4.2

1296688 2002, Adsorption/desorption of [dihydrofuranon-3-14C]BSN 2060 on four different soil, IM1981, DACO: 8.2.4.2

1296690 2000, Leaching potential of aged [dihydrofuranon-3-14C] BSN 2060 residues in Hesperia sandy loam, Bayer Corporation, 109483, DACO: 8.2.4.3.2

1296691 2001, Adsorption/desorption of 14C-BSN 2060-4-carboxy on four different soils, IM1991, DACO: 8.2.4.2

1296706 2001, Estimation of the adsorption coefficients (K_{oc}) of BSN 2060, BSN 2060-cyclobutyl and BSN 2060-enol photoisomers on soil using high performance liquid chromatography (HPLC), Bayer Corporation, 110750, DACO: 8.2.4.2

1296707 2002, Mobility determination of BSN 2060 by soil thin-layer chromatography in four soils, Bayer Corporation, 110342, DACO: 8.2.4.4

1296708 2001, Soil column leaching of BSN 2060, Bayer AG, MR-362/00, DACO: 8.2.4.3.1

1296498 2002, Acute toxicity of BSN 2060 technical to the sheepshead minnow (Cyprinodon variegatus) under flow-through conditions, Bayer Corporation, 110974, MRID: 45819708, DACO: 9.5.2.3

1296499 2002, Acute toxicity of BSN 2060 technical to the fathead minnow (Pimephales promelas) under flow-trough conditions, Bayer Corporation, 110975, MRID: 45819709, DACO: 9.5.2.3

1296500 2002, BSN 2060 - Life-cycle toxicity test with mysids (Americamysis bahia), 111024, MRID: 458197-11, DACO: 9.4.5

1296501 2002, Tier 2 seedling emergency and vegetative vigor nontarget phytotoxicity study using BSN 2060 SC 240, Bayer Corporation, 110325, MRID: 458196-29, DACO: 9.8.4

1296502 2002, Chronic toxicity of BSN 2060 240 SC to the waterflea (Daphnia magna) under a two pulse exposure regime, Bayer CropScience, 110992, MRID: 45819710, DACO: 9.3.3

1296503 2002, BSN 2060 240 SC extended laboratory test to assess effects on a population of Daphnia magna under a two pulse exposure regime, Bayer Corporation, 200062, MRID: 458197-13, DACO: 9.3.4

1296504 2004, BSN 2060 techn. ai.: Effects of a subchronic dietary exposure to the northern bobwhite quail including effects on reproduction and behaviour, Bayer AG, BAR/REP003, MRID: 45819724, DACO: 9.6.3.1

1296507 2002, Tier 1 seedling emergence and vegetative vigor nontarget phytotoxicity study using BSN 2060 SC 240, Bayer Corporation, 110851, MRID: 458197-06, DACO: 9.8.4

1296508 2002, Toxicity of BSN 2060 technical to duckweed (Lemna gibba G3), Bayer Corporation, 200072, MRID: 458197-14, DACO: 9.8.5

1296532 2002, BSN 2060 - The full life-cycle toxicity test with fathead minnow (Pimephales promelas), 13507.6138, MRID: 458197-12, DACO: 9.5.3.1

1296533 2001, BSN 2060 enol (BSN 0546)- Early life-stage toxicity test with rainbow trout (Oncorhynchus mykiss), 13507.6136, MRID: 458196-27, DACO: 9.5.3.1

1296534 2001, BSN 2060 - Early life stage toxicity to rainbow trout (Oncorhynchus mykiss) under flow-through conditions, Bayer AG, DOM 99124, MRID: 45819727, DACO: 9.5.3.1

1296541 2000, BSN 2060 a.i. - Acute effects on the honeybee Apis mellifera (Hymenoptera, Aphidae), 200196, MRID: 45819718, DACO: 9.2.4.1,9.2.4.2

1296542 2000, BSN 2060 SC 240 - Acute effects on the honeybee Apis mellifera (Hymenoptera, Apidae), 200195, MRID: 45819717, DACO: 9.2.4.1,9.2.4.2

1296547 1999, Acute toxicity of BSN 2060 (tech.) to earthworms (Eisenia fetida), Bayer AG, HBF/RG 292, DACO: 9.2.3.1

1296548 1999, Influence of BSN 2060 (tech.) on development and emergence of larvae of Chironomus riparius in a water-sediment system, Bayer AG, HBF/CH 32, MRID: 45819728, DACO: 9.3.4

1296549 1999, Influence of BSN 2060 SC 240 on the reproduction of earthworms (Eisenia fetida), Bayer AG, HBF/RG 304, MRID: 45819732, DACO: 9.2.3.1

1296550 1999, BSN 2060 techn.ai.: Acute oral toxicity for bobwhite quail (Colinus virginianus), Bayer AG, BAR/LD026, MRID: 458197-23, DACO: 9.6.2.1

1296551 1999, Acute toxicity of BSN 2060 SC 240 to water fleas (Daphnia magna), Bayer AG, HBF/DM 213, MRID: 45819729, DACO: 9.3.2

1296552 1999, Acute toxicity of BSN 2060 SC 240 to earthworms (Eisenia fetida), Bayer AG, HBF/RG 311, MRID: 45819733, DACO: 9.2.3.1

1296553 1999, BSN 2060 SC 240 - Acute toxicity (96 hours) to rainbow trout (Oncorhynchus mykiss) in a static test, Bayer AG, DOM 99024, DACO: 9.5.2.1

1296554 1999, BSN 2060 SC 240 - Acute toxicity (96 hours) to bluegill (Lepomis macrochirus) in a static test, Bayer AG, DOM 99088, MRID: 45819726, DACO: 9.5.2.2

1296555 2000, Acute toxicity of BSN 2060-enol to water fleas (Daphnia magna), Bayer AG, HBF/DM 219, MRID: 45819730, DACO: 9.3.2

1296556 2000, Acute toxicity of BSN 2060-Enol to rainbow trout (Oncorhynchus mykiss) in a 96-hour static test, 737392, MRID: 45819628, DACO: 9.5.2.1

1296557 2000, Toxicity of BSN 2060-Enol to Pseudokirchneriella subcapitata (formerly Selenastrum capricornutum) in a 96 hour algal growth inhibition test, 737414, DACO: 9.8.2

1296558 2001, 14C-BSN 2060 - Bioconcentration in rainbow trout, BAG 317/994679, DACO: 9.5.6

1296559 2000, Acute toxicity of BSN 2060 technical to the waterflea (Daphnia magna) under static conditions, Bayer Corporation, 109247, MRID: 45854512, DACO: 9.3.2

1296560 2002, Toxicity of BSN 2060 technical to the green alga Selenastrum capricornutum, Bayer Corporation, 110407, MRID: 45819703, DACO: 9.8.2

1296561 2002, Acute toxicity of BSN 2060 technical to the bluegill (Lepomis macrochirus) under flow-through conditions, Bayer Corporation, 110408, MRID: 458197-04, DACO: 9.5.2.2

1296562 2002, Acute toxicity of BSN 2060 technical to the rainbow trout (Oncorhynchus mykiss) under flow-through conditions, Bayer Corporation, 110970, MRID: 110970, DACO: 9.5.2.1

1296563 2002, Chronic toxicity of BSN 2060 enol to the waterflea (Daphnia magna) under flow-through conditions, Bayer Corporation, 110349, MRID: 45819701, DACO: 9.3.3

1296564 2002, Chronic toxicity of BSN 2060 technical to the waterflea (Daphnia magna) under flow-through conditions, Bayer Corporation, 110612, MRID: 458197-05, DACO: 9.3.3

1296565 2001, Avian reproduction study with BSN 2060 technical in mallard ducks (Anas platyrhynchos), 110119, MRID: 45819626, DACO: 9.6.3.2

1296567 2002, BSN 2060 techn.: 5-day-dietary LC_{50} to bobwhite quail (Colinus virginianus), Bayer AG, BAR/LC004, DACO: 9.6.2.4

1296568 2002, BSN 2060 techn.: 5-day-dietary LC_{50} to mallard duck (Anas platyrhynchos), Bayer AG, BAR/LC008, MRID: 458197-22, DACO: 9.6.2.5

1296728 2001, BSN 2060 - Acute toxicity to eastern oystern (Crassostrea virginica) under flow-through conditions, 110199, DACO: 9.4.2

12967291431963 2001, BSN 2060 - Acute toxicity to mysids (Americamysis baihia) under flow-through conditions, 110404, MRID: 45819702, DACO: 9.4.2

Response to PMRA review of spiromesifen, DACO: Response to Comments

5.0 Value

PMRA Number — Reference

1296301 Forbid 240 SC Insecticide/Acaricide (240 g a.i./L spiromesifen) for the control of insects and mites on fruit, ornamentals and vegetables grown outdoors or in greenhouses

1296303 Efficacy summary trials

1342491 The biological profile of spiromesifen (Oberon) - A new tetrinic acid insecticide-acaricide