

CALIFORNIA DEPARTMENT OF PESTICIDE REGULATION
PUBLIC REPORT 2005-2

Spiromesifen

Tracking ID Numbers CRR-200427N thru CRR-200430N

DESCRIPTION OF ACTION

Bayer Environmental Science, A Business Group of Bayer CropScience, LP (Bayer Environmental) submitted applications seeking California registration of BSN 2060 480SC (BSN 2060), EPA Reg. No. 432-1280, and Forbid 4 F Ornamental Insecticide/Miticide (Forbid 4 F), EPA Reg. No. 432-1279. Additionally, Bayer CropScience LP (Bayer CropScience) submitted applications seeking California registration of Spiromesifen Technical, EPA Reg. No. 264-718 and Oberon 2 SC Insecticide/Miticide (Oberon 2 SC), EPA Reg. No. 264-719 to control mites and whiteflies. These products contain the new active ingredient spiromesifen.

The Department of Pesticide Regulation (DPR) evaluated the product labels and scientific data supporting registration of these products and found them to be acceptable to support conditional registration. The acute health risks from exposure to spiromesifen are minimal due in part to its low mammalian toxicity. Precautionary and first aid statements on the product labels, as well as label directions requiring personal protective equipment (PPE) and other protective measures adequately mitigate potential health risks to persons who may come in contact with the pesticide. DPR does not expect significant adverse environmental impacts to result from registration of these products. DPR accepted both Bayer Environmental and Bayer CropScience applications for registration concurrently with their submission of applications to the United States Environmental Protection Agency (U.S. EPA) for federal registration. U.S. EPA registered Spiromesifen Technical, Oberon 2 SC, Forbid 4 F, and BSN 2060 on May 3, 2005.

BACKGROUND

Registrants:	Bayer Environmental and Bayer CropScience
Common name:	Spiromesifen
Chemical name:	2-oxo-3-(2,4,6-trimethylphenyl)-1-oxaspiro[4,4]non-3-en-4-yl 3,3-dimethylbutanoate
Brand names:	Spiromesifen Technical, BSN 2060, Forbid 4 F, and Oberon 2 SC
Uses:	To control mites and whiteflies on minor crops (Oberon 2 SC), ornamental plants, flowers, and foliage plants (Forbid 4 F), ornamental plants, flowers and foliage plants in the greenhouse and field and container nurseries (BSN 2060).
Pests controlled:	Whiteflies, spider mites and other mites
Type of registration:	Conditional - BSN 2060, Forbid 4 F, and Oberon 2 SC.

Spiromesifen belongs to a new class of pesticides, the keto-enols. The keto-enols are derivatives of tetrone acid (spirocyclic tetrone acids) and are reported to act through inhibition of lipid biosynthesis. This active ingredient works on all developmental stages of mites. However, mite

juvenile stages are more susceptible than adults. The active ingredient is also effective against whitefly nymphs and pupal stages.

Spiromesifen Technical is a liquid concentrate containing 96.99% active ingredient intended solely for use in the manufacturing of pesticide products.

Oberon 2 SC is formulated as a liquid suspension with 23.1% spiromesifen. The label recommends use on field corn, cotton, strawberry, cucurbit, fruiting, leafy, brassica, tuber, and corm vegetables. It can be applied by air, ground equipment or through chemigation. Thorough coverage of all plant parts is required and timing must be based on careful scouting and local thresholds. The label recommends application of 5.7 to 8.5 fluid ounces per acre on field corn with a preharvest interval (PHI) of 5 days. The rate of application on vegetable crops (cucurbit, fruiting, leafy, and brassica) is 7.0 to 8.5 fluid ounces per acre with a PHI of 7 days. Oberon 2 SC use on cotton is recommended at 6.0 fluid ounces per acre for early season applications. Mid-late season application is recommended at 8.0 to 16.0 fluid ounces per acre. The PHI for cotton is 30 days. The recommended rate of application on strawberry is 12.0 to 16.0 fluid ounces per acre with a three day PHI.

BSN 2060 is a flowable concentrate containing 45.2% spiromesifen. It can be applied by ground equipment at 2 to 4 fluid ounces per 100 gallons of spray solution on ornamental plants, flowers and foliage plants in the greenhouse and field and container nurseries. Each application should be timed when the whitefly or mite population begins to build and before a damaging population becomes established not to exceed four times per season.

Forbid 4 F is a liquid suspension containing 45.2% spiromesifen. It can be applied by ground equipment at 2 to 4 fluid ounces per 100 gallons of spray solution on shrubs, trees (including non-bearing fruit trees), flowers and foliage plants in outdoor landscapes. It is more effective against the egg and nymphal stages of whiteflies and mites. As such, it should be applied during this period not to exceed three times per season.

SCIENTIFIC REVIEW

A. Chemistry

1. Product Chemistry: DPR evaluated the submitted chemistry studies for Spiromesifen Technical, BSN 2060, Forbid 4 F, and Oberon 2 SC and summarized the results in Tables I through III.

Table I. Physical and Chemical Properties Using Spiromesifen Technical as the Test Substance

Properties	Values
Color	Colorless
Physical State	Crystals
Odor	Intense, Characteristic
Storage Stability	Stable for two years in HDPE container at ambient temperature.
pH	5.19 (2% suspension)
Viscosity	Solid at room temperature.
Density	0.13 g/cm ³ at 21°C
Partition Coefficient	log P _{ow} = 4.55 at 20°C
Solubility (water)	0.13 mg/L
Vapor Pressure	7x10 ⁻⁶ Pa at 20°C
Henry's Law Constant	2x10 ⁻² Pa m ³ /mol

Table II. Physical and Chemical Properties Using BSN 2060 as the Test Substance

Properties	Values
Physical state	Liquid
Density	1.08 g/mL at 20/20°C
pH	3.9 (10% w/v solution)
Flammability	Not combustible
Viscosity	884 cps at 25°C

Table III. Physical and Chemical Properties Using Oberon 2 SC as the Test Substance

Properties	Values
Physical state/color/odor	Viscous liquid/light/tan/musty, earthy odor with bleach like accent.
Density (20°C)	1.029 g/mL
pH (10% aqueous solution)	4.6
Flammability	Not flammable
Nominal Concentration	23.1%

DPR found the product chemistry data to be satisfactory to meet the regulatory data requirements to support the registration of these products.

2. Residues in Food and Animal Feed: Adequate confirmatory method validation and independent method validation were submitted for residue analytical methods conducted with Oberon 2 SC.
3. Environmental Fate: The spiromesifen environmental fate studies, which included: adsorption/desorption, hydrolysis, photolysis (aqueous and soil), soil metabolism (aerobic and anaerobic), field dissipation studies, and U.S. EPA Data Evaluation Reports were reviewed and found to be satisfactory.

The K_{oc} values from the soil adsorption/desorption studies using Thin Layer Chromatography ranged from 45,296 to 106,195 indicating spiromesifen has low mobility in soil. The hydrolysis study was conducted in water with pH levels at 4, 7, and 9 for a period of 30 days at 25°C. Under alkaline conditions, spiromesifen hydrolyzes readily with a half-life of 4.3 days (estimated from linear regression). However, in neutral to acidic conditions, spiromesifen resists hydrolysis with a half-life of 24.8-53.3 days. In neutral water, spiromesifen is stable in the presence of sunlight (photolysis) and has a half-life of 86.6 days. However, in acidic water, spiromesifen degrades rapidly with a half-life of 1.7 days. The soil photolysis study was conducted in neutral conditions (pH 7.2). The estimated half-life of spiromesifen in sandy loam soil is 23.1 days (linear regression). The aerobic soil metabolism study indicated (through linear regression) that spiromesifen is relatively unstable with a half-life of 11.6 to 48.8 days. Similarly, with aquatic conditions, the aerobic metabolism of spiromesifen in sediments is 12.3 to 17.7 days. In anaerobic soil conditions, the estimated half-life (linear regression) was 17.6 days. Four terrestrial field dissipation studies were reviewed and the results indicate spiromesifen has a short half-life in soil as determined by first order linear regression. The study conducted in California reported 2.1 days. Similarly, the Washington field dissipation study reported 4.5 days; Texas reported 4.6 days; and Florida 6.4 days. Spiromesifen was generally retained in the top 15 cm of soil in the terrestrial field dissipation studies; however, the transformation products BSN2060-enol and BSN2060-carboxy were generally detected at the lowest depths of the field studies.

The submitted product and environmental fate data support registration of the subject products. The data indicate spiromesifen is unlikely to leach into groundwater because its water solubility is low and it is bound tightly to soil particles. In the soil spiromesifen dissipates readily and should not accumulate. The use of spiromesifen is expected to have minimal impact on the environment and it is not expected to leach into groundwater.

B. Toxicology

Bayer Environmental submitted adequate toxicology studies to conduct a complete toxicological evaluation studies for Spiromesifen Technical, BSN 2060, Forbid 4 F, and Oberon 2 SC. DPR evaluated the submitted data to ascertain the potential for adverse health effects. The acute toxicity parameters for Spiromesifen Technical and BSN 2060 are summarized in Tables IV and V respectively.

Table IV. Acute Toxicity of Spiromesifen Technical

Type of Study	Acute Toxicity Values	Acute Toxicity Category
Acute oral	LD ₅₀ >2000 mg/kg	III
Acute dermal*	LD ₅₀ >2000 mg/kg	III
Acute inhalation	LC ₅₀ >4.87 mg/l	IV
Primary eye irritation	No Irritation	IV
Primary dermal irritation	Negative	IV
Dermal sensitization	Potential Sensitizer	A dermal sensitizer
Signal word	Not Applicable	CAUTION

*Reported value. Submitted study unacceptable but upgradeable.

Table V. Acute Toxicity of BSN 2060

Type of Study	Acute Toxicity Values	Acute Toxicity Category
Acute oral	LD ₅₀ >2000 mg/kg	III
Acute dermal	LD ₅₀ >2000 mg/kg	III
Acute inhalation	LC ₅₀ >1.84 mg/l	III
Primary eye irritation	Slight Irritation	IV
Primary dermal irritation	Primary dermal irritation index = 0.5	IV
Dermal sensitization	No dermal responses	Not a dermal sensitizer
Signal word	Not Applicable	CAUTION

DPR's evaluation of the acute toxicity studies indicates that these spiromesifen products are low in mammalian toxicity. DPR toxicologists determined that the differences in formulations between the two end-use products and BSN 2060 were unlikely to be of toxicological concern. Acute toxicity studies conducted with BSN 2060 are suitable for bridging to the two end-use products. The precautionary language on the product labels adequately identifies the acute toxicity hazards noted in the studies.

DPR found the submitted toxicology studies sufficient to satisfy the data requirements of the Birth Defects Prevention Act (SB 950). Because neurotoxic symptoms were not observed during the acute and subchronic neurotoxicity studies, an acceptable developmental neurotoxicity study is not required at this time. As a result of these findings, DPR has placed spiromesifen in "low" priority for conducting a risk assessment. DPR prioritizes pesticide active ingredients for risk assessment based on the nature of the potential adverse health effects, number of potential adverse health effects, number of species affected, NOELs, potential for human exposure, use patterns, and similar factors. Based on these criteria, pesticides with the greatest potential for health problems are placed in high priority, with other chemicals being placed in moderate or low priority. The purpose of the risk assessment will be to appraise the potential for spiromesifen to cause adverse health effects in humans if exposed to the pesticide as the result of a legal use. Further toxicity information is available in DPR's Summary of Toxicology Data for spiromesifen, available on DPR public website at <http://www.cdpr.ca.gov/docs/toxsums/pdfs/5858.pdf>.

C. Health & Safety

An evaluation of the medical management information on the BSN 2060, Forbid 4 F and Oberon 2 SC labels and the acute toxicity study results indicate the product labels bear all of the required statements and warnings regarding safety to handlers and other persons who may be exposed to the pesticide. The product labels bear an adequate first aid statement. In addition, the labels require persons mixing and loading BSN 2060, Forbid 4 F and Oberon 2 SC to wear long-sleeved shirt and long pants, chemical-resistant gloves category A (such as natural rubber) and shoes plus socks. Applicators must wear long-sleeved shirt, long pants, shoes plus socks. Following application, workers are not allowed to enter treated areas during the restricted entry interval (REI) of 12 hours. Personal Protective Equipment (PPE) is required for early entry to treated areas that is permitted under the Worker Protection Standard and that involves contact with anything that has been treated include coveralls worn over short sleeved shirt and short pants, chemical resistant gloves, and shoes plus socks.

D. Fish & Wildlife

The registrant submitted fish and wildlife toxicity studies, including studies on honeybee, bobwhite quail, earthworm, *Daphnia magna* (water fleas), bluegill sunfish, minnow (fathead and sheepshead), mysid shrimp, oyster, and rainbow trout. The submitted data are adequate to characterize the toxicity to wildlife and aquatic animals from environmental exposure. Table VI summarizes the results of these studies.

Table VI. Summary of Toxicity Studies for Wildlife*

Test Animal	Type of Study	Acute Toxicity Value**	Relative Toxicity
Honeybee	Contact study (48 hrs.)	>200 µg a.i./bee (LD ₅₀)	Relatively non-toxic
Honeybee	Feeding study (48 hrs.)	792.4 µg a.i./bee (LD ₅₀)	Relatively non-toxic
Bobwhite quail	Single acute oral dose	>2000 mg/kg (LD ₅₀)	Relatively non-toxic
Earthworm	Soil exposure (14 days)	>1000 mg (LD ₅₀)	Relatively non-toxic
<i>Daphnia magna</i>	Water exposure (48 hrs.)	>92.3 µg a.i./l (LC ₅₀)	Slightly toxic
Bluegill sunfish	Water exposure (96 hrs.)	>33.7 µg a.i./l (LC ₅₀)	Slightly toxic
Fathead minnow	Water exposure (96 hrs.)	>40.1 µg a.i./l (LC ₅₀)	Slightly toxic
Mysid shrimp	Water exposure (96 hrs.)	>76 µg a.i./l (LC ₅₀)	Slightly toxic
Oyster	Water exposure (96 hrs.)	>26 µg a.i./l (EC ₅₀)	Slightly toxic
Rainbow trout	Water exposure (96 hrs.)	15.5 µg a.i./l (LC ₅₀)	Slightly toxic
Sheepshead minnow	Water exposure (96 hrs.)	>46.3 µg a.i./l (LC ₅₀)	Slightly toxic

*The test substance used for the studies was BSN 2060 Technical.

** Acute toxicity values expressed as:

a. LD₅₀=lethal dose that will kill 50% of test population,

- b. LC₅₀=lethal environmental concentration that will kill 50% of test population, and
- c. EC₅₀=concentration that caused some effect that can lead to death.

The data indicate spiromesifen is relatively non-toxic to terrestrial wildlife, and slightly toxic to fish, oysters, and aquatic invertebrates. Label directions bear a warning indicating that the product is toxic to birds, fish and aquatic organisms and prohibit application of the product directly to water, to areas where surface water is present or to intertidal areas below the mean high water mark. A surface water advisory alerts applicators of the potential for this product to contaminate water through runoff or through drift of spray in wind. Labeling for BSN 2060, Oberon 2 SC, and Forbid 4F recommend maintaining a level vegetative buffer strip between areas to which the products are applied and surface water features such as ponds, streams, and springs will reduce the potential for contamination of water from runoff.

Based on the submitted data, registered uses, label rates, and use restrictions for spiromesifen, DPR does not expect toxic concentrations to occur in aquatic environments from use of the product in accordance with label directions.

E. Efficacy & Phytotoxicity

Submitted field data were limited, but adequate to demonstrate the ability of spiromesifen to control whiteflies and mites on ornamental plants, flowers, foliage plants, field corn, cotton, cucurbit vegetables, fruiting vegetables, leafy vegetables, tuber vegetables and strawberries. Some phytotoxicity was noted in the form of leaf cupping and development delays on several plants. These effects were outgrown in weeks but in the case of pelargonium and geraniums it was significant enough to warrant the label statement recommending against use on these plants on the label. In addition, the label advises that before using any tank mix, the user should test the combination on a small portion of the crop to be treated, to ensure that a phytotoxic response will not occur as result of application. Conditional registration was granted for one year to gather additional phytotoxicity data on more representative sampling of ornamentals. Additional data are also needed to support the claim of whitefly control on shrubs, trees, flower, and foliage plants. Additionally, efficacy data are needed to demonstrate control of mites and whiteflies utilizing chemigation method of application.

ALTERNATIVES

Spiromesifen will introduce a new chemical class (keto-enols) and a new mode of action (inhibition of lipid biosynthesis). Spiromesifen has been tested in many programs as a stand-alone product. It provides a reliable high level of performance equal to or better than the efficacy and residual control provided by current standards.

Performance and positioning will ensure that growers adopt this new class of chemistry to replace older miticides and whitefly insecticides. Competitors vary depending upon pest and crop but the major products used for mite control are abamectin, bifenthrin, hexythiazox, dimethoate, dicofol and propargite, while for whitefly control they are acetamiprid, buprofezin, acephate, chlorpyrifos and endosulfan. The introduction of spiromesifen will bring many desirable benefits, including: a favorable human safety profile that will reduce risks to human

health; a favorable environmental profile that will reduce the environmental burden and the risk for contamination of ground water and surface water; a much needed and efficacious resistance management tool for both mite and whitefly control; an excellent fit in integrated pest management strategies; and compatibility with genetically modified crops.

CONCLUSION

DPR evaluated the product labels and scientific data submitted to support the registration of Spiromesifen Technical, BSN 2060, Forbid 4 F, Oberon 2 SC and found them acceptable to support conditional registration. The acute health risks to humans from exposure to spiromesifen are minimal due to its low mammalian toxicity. The precautionary and first aid statements on the product labels, as well as the required PPE and other protective measures, mitigate potential health risks to persons who may be exposed to the pesticide. If, after the risk assessment, DPR determines that exposure to spiromesifen results in unacceptable margins of exposure, further restrictions will be placed on the use of spiromesifen at that time. Submitted data also indicate that no significant adverse environmental impacts are expected to occur from the use of BSN 2060, Forbid 4 F and Oberon 2 SC and that when used in accordance with label directions, the product will be effective for its intended use.

Conditional registration is proposed for BSN 2060, Forbid 4 F, and Oberon 2 SC. Before the individual products will be registered unconditionally in California, the applicant must provide the following: BSN 2060 and Forbid 4 F require additional phytotoxicity data on a more representative sampling of ornamentals as well as efficacy data to support the claim of whitefly control on shrubs, trees, flower, and foliage plants in outdoor landscape. Oberon 2SC requires product efficacy data utilizing chemigation as a method of application.