



**US Environmental Protection Agency
Office of Pesticide Programs**

Petition for Spiromesifen

November 14, 2007

exclusive use 3 extra 3 years

Bayer CropScience

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November 14, 2007

Document Processing Desk
Office of Pesticide Programs (7504C)
U.S. Environmental Protection Agency
One Potomac Yard
2777 South Crystal Drive (7505P)
Arlington, VA 22202

Attention: Mr. Tom Harris, RD

Re: Petition for 3 Years Extension of Exclusive Data Use for Spiromesifen
(EPA Reg. No. 264-718) as provided for Under FIFRA Section 3(c) (1) (F)
(ii)

Bayer CropScience
RTP
P. O. Box 12014
RTP, NC 27709
Tel. 919 549-2000

Dear Mr. Harris,

Bayer CropScience hereby petition EPA to extend the period of exclusive data use for **spiromesifen** insecticide by 3 years, by applying the provision of FIFRA Section 3(c) (1) (F) (ii).

Bayer CropScience believe that spiromesifen meets all of the criteria required for this provision based on currently registered uses.

Spiromesifen has been classified as a reduced risk compound by EPA. Residue studies supporting registration are available for 11 minor crops, thus qualifying for 3 additional year data exclusivity (1 year for 3 minor uses up to a maximum of 3 years) providing the other criteria listed in FIFRA Section 3(c) (1) (F) (ii) are met. Details of how spiromesifen meets each of these criteria is described in attached petition.

I copied Robert Perlis of the Office of General Counsel, as instructed by Barbara Madden e-mail to Jamin Huang on 8/25/05. If this petition needs to be forwarded to any other person/division within the Agency, would you please see that it can be done.

If you have any question, please contact me either by telephone at 919-549-2156 or email at sherry.movassaghi@bayercropscience.com.

Sincerely,

Sherry Movassaghi, Ph.D.
Registration Product Manager

Petition for 3 Years Extension of Exclusive Data Use for Spiromesifen as Provided for Under FIFRA Section 3(c) (1) (F) (ii)

Bayer CropScience hereby petition EPA to extend by 3 years the period of exclusive data use for spiromesifen insecticide by applying the provision of FIFRA Section 3(c) (1) (F) (ii).

FIFRA Section 3(c) (1) (F) (ii) states that:

The period of exclusive data use provided under clause (i) shall be extended 1 additional year for each 3 minor uses registered after the date of enactment of this clause and within 7 years of the commencement of the exclusive use period, up to a total of 3 additional years for all minor uses registered by the Administrator if the Administrator, in consultation with the Secretary of Agriculture, determines that, based on information provided by an applicant for registration or a registrant, that -

- (I) there are insufficient efficacious alternative registered pesticides available for the use;*
- (II) the alternatives to the minor use pesticide pose greater risks to the environment or human health;*
- (III) the minor use pesticide plays or will play a significant part in managing pest resistance; or*
- (IV) the minor use pesticide plays or will play a significant part in an integrated pest management program.*

Bayer CropScience consider that spiromesifen meets all of the criteria listed above as described in this document based on currently registered uses. Spiromesifen and its formulated products OBERON® 2 SC Insecticide/Miticide, OBERON® 4 SC Insecticide/Miticide and Forbid 4F Insecticide/Miticide has brought a new mode of action to the crops on which it is registered and has the unique property of controlling both mites and whiteflies. Formulated spiromesifen was first registered by U.S. EPA on May 3, 2005 following tolerances having been set on the crops and crop groups below on April 27, 2005:

- Cotton
- Field corn
- Strawberries
- Tuberous and corm vegetables (EPA crop subgroup 1-C)
- Vegetable, leafy greens subgroup (EPA crop subgroup 4-A)
- Vegetables, brassica, head and stem subgroup (EPA crop subgroup 5-A)
- Vegetables, brassica, leafy greens subgroup (EPA crop subgroup 5-B)
- Fruiting vegetables (EPA crop group 8)
- Cucurbit vegetables and melons (EPA crop group 9)

To support the above registrations residue trials were conducted in the major use crops of corn, cotton, tomatoes and potatoes and on a wide range (eleven) of minor crops to support the numerous minor use crops on which spiromesifen is currently registered. The minor use crops for which residue data is available are listed in Table 1.

Table 1 Minor Use Crops on which Residue Studies Have Been Conducted

Crop	MRID #	Crop Group/Subgroup
Strawberries	45819411	none
Head Lettuce	45819427	4-A
Leaf Lettuce	45819427	4-A
Spinach	45819427	4-A
Broccoli	45819426	5-A
Cabbage	45819426	5-A
Mustard Greens	45819431,46722301	5-B
Peppers	45819417	8
Cantaloupe,	45819414	9
Cucumbers	45819414	9
Summer Squash	45819414	9

Residue studies supporting registration are, therefore available for 11 minor crops, thus qualifying for 3 years data exclusivity (1 year for 3 minor uses up to a maximum of 3 years) providing the other criteria listed above are met. Details of how spiromesifen meets each of these criteria is described below. On November 28, 2006 EPA's Reduced Risk Committee granted, retrospectively after review of the complete package, reduced risk status to spiromesifen for use on all registered crops, namely cotton, cucurbits, field corn, fruiting vegetables, Brassica leafy vegetables, leafy vegetables (non-Brassica), strawberry, tuberous vegetables and greenhouse, landscape, and nursery ornamentals. The reduced risk submission (Kelly, I. et al., 2006; Arthur, E. et al., 2003a; Buckelew, L. and J. Mixson. 2003) and the supplementary response (Arthur, E. et al., 2003b) provides supporting documentation to the information below.

Criterion I: There are insufficient efficacious alternative registered pesticides available for the use

In the reduced risk document a summary of major competitor insecticides/miticides registered for mite and/or whitefly control at the time of submission was listed. Spiromesifen is a unique compound that controls both whiteflies and mites. While this confers reduced risk advantages, it means that the competitors are very different dependent on the pest being controlled. Competitors (by active ingredient) were selected that accounted for more than 5% of the foliar treated acres in a particular crop/crop group for either whitefly or mite control. Soil applied systemic chemistries such as aldicarb (Temik®) in the mite market and imidacloprid (Admire®) and thiamethoxam (Platinum®) in the whitefly market were not included as spiromesifen will not compete in or affect these markets. Generally, competitors were only selected if they are labeled for the same pests that are on the spiromesifen (OBERON®) label. In addition to products that were used in greater than 5% of treated acres, recently registered products that were anticipated to capture significant market share were included. Buprofezin (Courier®), hexythiazox (Savey®) and acetamiprid (Assail®) fell into this category. The competitors are listed in Table 2.

Table 2 Competitors to Spiromesifen in Minor Use Crops

Crop/ Crop Group	Pest	Active Ingredient	Product Name	Chemical Class/Family
Strawberry	Mites	Spiromesifen	OBERON® 2 SC	Cyclic ketoenol
		Abamectin	Agri-Mek® 0.15EC	Avermectin, macrocyclic lactone
		Hexythiazox	Savey® 50 DF	Carboxamide
	Whiteflies	Spiromesifen	OBERON® 2 SC	Cyclic ketoenol
Melon/Cucurbit	Whiteflies	Spiromesifen	OBERON® 2 SC	Cyclic ketoenol
		Buprofezin	Courier®™ IGR	Substituted thidiazinone
		Endosulfan	Thiodan® 3EC	Chlorinated hydrocarbon
Vegetables, Fruiting	Mites	Spiromesifen	OBERON® 2 SC	Cyclic ketoenol
		Abamectin	Agri-Mek® 0.15EC	Avermectin, macrocyclic lactone
		Dicofol	Kelthane® MF	Organochlorine
	Whiteflies	Spiromesifen	OBERON® 2 SC	Cyclic ketoenol
		Acetamiprid	Assail®™ 70WP	Chloronicotinyl
		Buprofezin	Courier®™ IGR	Substituted thidiazinone
		Endosulfan	Thiodan® 3EC	Chlorinated hydrocarbon
Pyriproxyfen	Knack® IGR	Juvenile hormone mimic		
Vegetables, leafy (Non- Brassica)	Whiteflies	Spiromesifen	OBERON® 2 SC	Cyclic ketoenol
		Acephate	Orthene® 75 S	Organophosphate
		Acetamiprid	Assail® 70WP	Chloronicotinyl
		Buprofezin	Courier®™ IGR	Substituted thidiazinone
Vegetables, leafy (Brassica)	Whiteflies	Spiromesifen	OBERON® 2 SC	Cyclic ketoenol
		Endosulfan	Thiodan® 3EC	Chlorinated hydrocarbon

As can be seen in Table 2 there are a limited number of competitors for each use and in some cases such as whiteflies in strawberries, essentially no viable alternatives. Mites are the larger market for spiromesifen and abamectin alone generally dominates this market. In addition field and laboratory tests have shown that spiromesifen provides consistent, long lasting pest control and other performance attributes which makes it superior to major competitors as shown in Table 3.

Table 3: Comparison of Spiromesifen Control to Major Competitive Products

Parameter	Product					
Active Ingredient	Spiromesifen	Abamectin	Dicofol	Hexythiazox	Pyriproxyfen	Acetamiprid
Trade Name	Oberon®	Zephyr® & Agri-Mek®	Kelthane®	Savey®	Knack®	Intruder™
Company	Bayer CropScience	Syngenta	Dow	Gowan	Valent	DuPont
Mode of Action	Lipid biosynthesis inhibitor	GABA receptor protein inhibitor	GABA-gated Cl channel antagonist	Electron transport inhibitor	Juvenile hormone mimic	Inhibition of nicotinic acetylcholine receptors
Residual Time	30-45 days	30-40 days	21 days	30 days	21-31 days	14-21 days
Pest /Benefit	Pest /Benefit					
Whitefly	+++	---	---	---	+++	+++
Spider Mite	+++	+++	++	++	---	---

+++	Excellent control
++	Good control
---	Poor control

Criterion II: The alternatives to the minor use pesticide pose greater risks to the environment or human health

Spiromesifen is a reduced risk compound. The toxicological findings of the Health Effects Division when registering spiromesifen were:

- Technical spiromesifen shows low acute toxicity (Toxicity Category III, IV) via the oral, dermal and inhalation routes of exposure.
- It is neither an eye nor dermal irritant (Toxicity Category IV), but showed moderate potential as a contact sensitizer in a Magnusson and Kligman maximization assay.
- An acute endpoint of concern attributable to a single exposure (dose) was not identified from the oral toxicity studies including infants and children
- Spiromesifen shows no significant developmental or reproductive effects
- Spiromesifen is not neurotoxic
- Spiromesifen is classified as "not likely to be carcinogenic to humans"

The reduced risk packages submitted to EPA provide supporting details as to why the alternatives to spiromesifen pose greater risks to both human health and the environment as summarized below.

Alternatives Pose Greater Risk to Human Health

Spiromesifen introduces newer, safer chemistry to control mite and whitefly infestations. Spiromesifen showed no evidence of oncogenicity and is classified as "unlikely to be a human carcinogen" (i.e. Class E oncogen). In the larger mite market, spiromesifen competitors are abamectin, dicofol, and hexythiazox. Of these products, only abamectin

has an E classification. The others are class C carcinogens with hexythiazox being regulated by linear extrapolation (Q1*). Spiromesifen showed no evidence of being a primary reproductive or developmental toxicant. Abamectin is a possible primary reproductive and/or neonatal toxicant. The end-use products of spiromesifen carry the signal word "Caution" being in Toxicity Category III. Abamectin carries the signal word "Warning" (Toxicity Category II).

In the whitefly market, spiromesifen competes with acephate, acetamiprid, buprofezin, endosulfan and pyriproxyfen. Acephate is classified as a possible C carcinogen, buprofezin is a possible primary reproductive and/or neonatal toxicant, endosulfan resulted in evidence of developmental toxicity at doses below that at which maternal toxicity was observed. Endosulfan formulation (Thiodan®) is Category I based on eye irritation potential carrying the signal word "Danger".

Alternatives Pose Greater Risk to the Environment

Risk assessments demonstrate that spiromesifen and its primary metabolites pose minimal risk to non-target organisms. Tier 1 risk quotients are generally below all levels of concern or can be easily refined to demonstrate negligible risk. Table 4 is a comparison based on Tier 1 risk quotients taken from the reduced risk submission in which quantitative values of these risk quotients are provided.

Table 4: Summary of Ecological Risk for Spiromesifen and Major Competitors

Chemical	Avian Acute	Avian Chronic	Mammal Acute	Mammal Chronic	Fish Acute	Fish Chronic	Daphnia Acute	Daphnia Chronic	Mysid Acute	Bees
Hexythiazox		- ^a				- ^a				
Pyriproxyfen										
Spiromesifen										
Acetamiprid								- ^a		
Buprofezin										
Abamectin								- ^a		
Dicofol								- ^a		
Acephate										
Endosulfan										

^a No data available
 = No Tier 1 LOC exceedences
 = Between the endangered species LOC and the high risk LOC for acute risk. Between 1 and 2 times the LOC for chronic risk
 = Greater than the high risk LOC for acute risk. Greater than 2 times the LOC for chronic risk.

Of the competitors only pyriproxyfen and acetamiprid in the whitefly market and possibly hexythiazox in the mite market have a potentially more favorable profile. In the larger mite market hexythiazox is a significant competitor only in strawberries where there are very few alternates, the only significant one being abamectin which has a much less favorable profile. While pyriproxyfen generally has a very safe overall profile, it poses a 20-fold greater chronic risk to daphnia than spiromesifen (Arthur, E. et al., 2003a). A strong case can therefore be made that spiromesifen has the safest overall ecological profile with the exception of the minor hexythiazox use in strawberries.

Spiromesifen has minimal effects on predacious bugs and other beneficials at typical use rates. It is practically non-toxic to pollinators.

Criterion III and IV: the minor use pesticide plays or will play a significant part in managing pest resistance (III); or the minor use pesticide plays or will play a significant part in an integrated pest management program (IV)

The USDA defines IPM as, "A sustainable approach to managing pests by combining biological, cultural, physical, and chemical tools in a way that minimizes economic, health, and environmental risks". Spiromesifen brings a new mode of action to all the crops it is registered on and has the unique property of controlling both mites and whiteflies. Resistance management is a critical component for whitefly and mite control and spiromesifen is an excellent fit.

Integrated pest management is improving in the crops on which spiromesifen will be used as newer "softer" products such as abamectin for mite control and the chloronicotinyls/neonicotinoids and insect growth regulators for whitefly control are established in the market. These newer products fit better with biological control methods and have precipitated substantial reductions in the use of organophosphates, pyrethroids and organochlorines in these crops. Control of spider mites with organophosphates and pyrethroids, particularly, has been problematic because these chemicals can stimulate mite reproduction and change plant physiology to make it a more suitable host. Additionally, in some areas resistance has developed to these insecticides.

Spiromesifen is an essential part of resistance management in regions where multiple crops are grown that are becoming increasingly dependent on the use of chloronicotinyls for whitefly control. The chloronicotinyl/neonicotinoid (CNI) class of chemistry has been used effectively for whitefly control in vegetables and melons since 1993, and it is an extremely important component to their production. In these crop complexes, insect growth regulators are the main products used to relieve the pressure towards chloronicotinyl resistance development.

Chloronicotinyls/neonicotinoids facing a particular threat for resistance development, particularly in the southwest, which will be a major use area for spiromesifen. Whitefly populations and subsequent generations of whiteflies occur across a diverse range of crops in the southwest. This presents a difficult problem for insecticide resistance management when similar chemistries are used in different commodities for the same pest. The University of Arizona has developed cross-commodity guidelines for this class of chemistry which emphasize the importance of chemical class rotation, where possible, to minimize selection pressure by the chemistries.

Furthermore, the discovery of the Q-biotype whitefly in the U.S could dramatically shift regional whitefly pest management. The Q-biotype whitefly is a new strain of *Bemisia tabaci* which is more commonly known as Sweetpotato whitefly or Silverleaf whitefly. This strain is visually indistinguishable from B-biotype whitefly but is known to be exceptionally less susceptible to the most common whitefly control products such as acetamiprid, buprofezin, imidacloprid, and thiamethoxam. However, lab studies have shown that spiromesifen is one, if not the only, very effective product on this very difficult to control pest (Guthrie, F. et al., 2003). Biological surveys of whiteflies from different regions of the U.S. have now confirmed detections of Q-biotype in the following states:

Alabama, Arizona, California, Connecticut, Florida, Georgia, Indiana, Kentucky, Louisiana, Michigan, New Jersey, New York, Oregon, Pennsylvania, and Vermont. So, Spiromesifen has a strong role in resistance management of whitefly, particularly the difficult to control Q-biotype.

Integrated pest management strategies clearly require additional chemical modes of action in the mite and whitefly market that fit with the objective of minimizing economic, health, and environmental risks if it is to be sustainable. The registration of spiromesifen has brought many desirable benefits, which fit with this objective.

Conclusions

In conclusion spiromesifen meets all the criteria for granting a 3 year extension of the exclusive data use period. Residue data is available for eleven minor use crops exceeding the required number of nine. The mite and whitefly market for the minor crops on which it is registered have very few valid alternatives and its adoption in the market place is showing that it is a valuable tool. EPA has granted it reduced risk status for all registered minor crops. It has no attributes of concern for human health in contrast to most competitors. It poses less risk to non-target organisms with the potential exception of hexythiazox in strawberries in which it is a valuable complementary tool.

Spiromesifen brings a completely new mode of action for both mite and whitefly control to all minor use product listed on label, including: strawberry, cucurbits/melons and vegetables (tuberous, fruiting and leafy, both non-brassica and brassica). Its level of control and residual efficacy is equal to or better than present standards. With its low use rate, long residual activity and dual pest activity, chemical use is minimized.

Spiromesifen will minimize resistance development to miticides for which there are very few effective competitors. Its use for whitefly control will minimize the development of resistance to the soil applied chloronicotinyls/neonicotinoids, a chemical class that is critical to growers. It will complement currently applied whitefly products such as insect growth regulators and pyrethroids that have already shown resistance development. It will also ensure that organophosphates and organochlorines, whose use has been diminishing, will not be re-introduced to combat this resistance. Spiromesifen has minimal effects on predacious bugs and other beneficials at typical use rates. It is practically non-toxic to pollinators.

References

Kelly, I., Bowers L., Christenson R, Arthur E., and Buckelew L. 2006. Justification for Designating Spiromesifen as a Reduced Risk Compound on Currently Registered Crops, EPA Pesticide Regulation Notice 93-7, Bayer CropScience, Research Triangle Park, NC. Report Number G201515. May 4, 2006, 8 pages. MRID # 46835601

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Reduced Risk Decision (Dated 10/ 17/2003) on Spiromesifen Use on Field Corn, Cotton, Vegetable and Fruit Crops, Cucurbit Vegetables, Fruiting Vegetables, Leafy Vegetables, Tuber Vegetables, Strawberry and Nursery Greenhouse and Landscape Ornamentals. Bayer CropScience Report Number G 200753.

Bucklew, L. and J. Mixson, 2003. Resistance Management, Comparative Performance, and Market Analysis for Spiromesifen: Oberon[®] 2 SC Insecticide/Miticide
Addendum Number 1 To: Reduced Risk Rationale for the Use of Spiromesifen on Field Corn, Cotton, Vegetable and Fruit Crops, Cucurbit Vegetables, Fruiting Vegetables, Leafy Vegetables, Tuber Vegetables, Strawberry and Nursery, Greenhouse and Landscape Ornamentals. Bayer CropScience Report Number 200566

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