Title

Petition for a Three-Year Extension of Exclusive Use Data Protection for Spirotetramat As Provided For Under FIFRA Section 3(c)(1)(F)(ii)

Data Requirement
Not Applicable

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Submitter: Sherry Movassaghi Date: 2013-08-23
(YYYY-MM-DD)

Typed Name of Submitter: Sherry Movassaghi

Typed Name of Company Bayer CropScience LP

The above statement supersedes all other statements of confidentiality that may occur elsewhere in this report.

GOOD LABORATORY PRACTICE COMPLIANCE STATEMENT

This report does not meet the requirements for EPA FIFRA Good Laboratory Practice Standards, 40 CFR Part 160, and differs in the following way:

(1) This report is not subject to Good Laboratory Practices.

Submitter: _____

Registration Manager
Bayer CropScience

Date: September 23, 2013

1.0 Introduction

Bayer CropScience, the sole registrant of the proprietary insecticide, spirotetramat, is hereby petitioning the Environmental Protection Agency for a three-year extension of exclusive use data protection, as provided under 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.

Further, in a Question & Answer document [http://www.epa.gov/pesticides/minoruse/#questions] concerning the exclusive use extension policy, the Agency clarifies that only one of the four criteria is necessary to qualify for consideration:

"To qualify to be considered under § 3(c)(1)(F)(ii) of FIFRA for an extension of the exclusive use period, the minor uses must be registered within the first 7 years from the start of the exclusive use period and meet one of the four criteria listed in FIFRA § 3(c)(1)(F)(ii)."

Additionally, in the same Question & Answer document, the Agency states that all minor-use crops contained in a given crop grouping potentially qualify for consideration:

"If the data for the representative crops in a crop grouping have been submitted and support establishment of the crop grouping, the Agency will count the non-representative minor crops within a crop grouping provided that they were registered within 7 years of the commencement of the initial exclusive use period for the active ingredient and the registrant is marketing the product for the minor crops. However, the non-representative minor crops must meet one of the four criteria identified in § 3(c)(1)(F)(ii) in order to be eligible to be considered for extension of exclusive use data protection."

As described in this petition, spirotetramat meets several of the criteria cited in FIFRA Section 3(c)(1)(F)(ii). Numerous regulatory approvals on minor-use crops have occurred within 7 years of the commencement of the exclusive use period; for the purposes of this document, only 53 will be discussed and discussions will center largely around three of the four of the criteria cited in FIFRA Section 3(c)(1)(F)(ii). Spirotetramat Technical (EPA Reg. No 264-1049) and three end-use products for crop markets, MOVENTO® (EPA Reg. No 264-1050), BYI 8330 150 OD Insecticide (EPA Reg. No. 264-1051), and ULTOR® (EPA Reg. No. 264-1065) were registered by the EPA on October 15, 2010.

EPA's Reduced Risk Committee has twice granted reduced risk status for spirotetramat. The initial submission (MRID 46904608 and 46904609) dated October 6, 2006 was granted reduced risk status on March 7, 2007 and the Tier 2 submission (MRID 47648214 and 47648215) dated February 11, 2009 was granted reduced risk status on May 19, 2009. A significant amount of information contained

within this document, specifically for discussions surrounding FIFRA Criterion II - the alternatives to the minor use pesticide pose greater risks to the environment or human health, has largely been taken from documents contained in the two reduced risk submissions.

2.0 Spirotetramat Minor Use Crop Candidates and Residue Data

Residue trials were conducted in crops and the crop group representative crops, including major and minor crops, to support the numerous minor crops on which spirotetramat is currently registered and appear on end-use product labels. Table 1 shows the 53 minor-use crop candidates included in this petition for extension of exclusive use of data and the corresponding residue data used to support the registration of these minor crops. Therefore, residue studies supporting registration are available on 53 minor use crop candidates.

IR-4 and various minor-use crop industries have shown a very high degree of interest in spirotetramat since learning of its unique properties and high degree of efficacy against target pests, as evidenced in the number of Product Clearance Requests received by IR-4 (1). Of the 53 minor crops listed in Table 1, five (dry bulb onion, globe artichoke, pomegranate, pineapple, and coffee) were submitted by external stakeholders as a Product Clearance Request to IR-4 and subsequently registered by EPA on May 2, 2013. In addition, while Section 3 registration was being pursued by IR-4 on dry bulb onion, Section 18 exemptions were requested each year by numerous onion-producing states and subsequently approved by EPA, demonstrating the need for spirotetramat as an effective rotational tool for effective resistance management of onion thrips.

All of the following 53 minor use crop candidates, supported by residue data from either individual crop or representative crops of crop groups, were registered within the requisite seven year period (prior to October 15, 2017) and added to the spirotetramat technical and various end-use product labels.

Table 1. Spirotetramat Minor-Use Crop Candidates

Candidate No.	Crop Candidate	Bearing / Harvested Acres 2011/2012[1]	Residue Data to Support	MRID #	Date Registered	Crop Group No.	Document Section Number
1	Grapefruit	73,400	Grapefruit	46904514	October 15, 2010	10	4.1
2	Lemon	55,000	Lemon	46904514	October 15, 2010	10	4.1
3	Lime	Not Listed	Orange, Grapefruit, Lemon	46904514	October 15, 2010	10	4.1
4	Key Lime	Not Listed	Orange, Grapefruit, Lemon	46904514	October 15, 2010	10	4.1
5	Kumquat	Not Listed	Orange, Grapefruit, Lemon	46904514	October 15, 2010	10	4.1
6	Pummelo	Not Listed	Orange, Grapefruit, Lemon	46904514	October 15, 2010	10	4.1
7	Tangerine	52,600	Orange, Grapefruit, Lemon	46904514	October 15, 2010	10	4.1
8	Tangelo	4,300	Orange,	46904514	October 15,	10	4.1

Candidate No.	Crop Candidate	Bearing / Harvested Acres 2011/2012[1]	Residue Data to Support	MRID #	Date Registered	Crop Group No.	Document Section Number
			Grapefruit, Lemon		2010		
9	Satsuma mandarin	Not Listed	Orange, Grapefruit, Lemon	46904514	October 15, 2010	10	4.1
10	Dry bulb onion	154,950	Dry bulb onion	48697608	May 2, 2013	3	4.2
11	Broccoli	128,500	Broccoli	46904509	October 15, 2010	5	4.3
12	Cabbage	65,900	Cabbage	46904509	October 15, 2010	5	4.3
13	Cauliflower	36,500	Cauliflower	46904509	October 15, 2010	5	4.3
14	Broccoli raab (rapini)	3,500[3]	Mustard Greens	46904509	October 15, 2010	5	4.3
15	Brussels sprouts	3,874[2]	Cabbage, Broccoli, Cauliflower	46904509	October 15, 2010	5	4.3
16	Cavalo broccolo	Not Listed	Cabbage, Broccoli, Cauliflower	46904509	October 15, 2010	5	4.3
17	Gai lon	Not Listed	Cabbage, Broccoli, Cauliflower	46904509	October 15, 2010	5	4.3
18	Bok choy	11,480[2]	Mustard Greens	46904509	October 15, 2010	5	4.3
19	Napa	11,480[2]	Cabbage, Broccoli, Cauliflower	46904509	October 15, 2010	5	4.3
20	Mustard cabbage (gai choy)	66[2]	Cabbage, Broccoli, Cauliflower	46904509	October 15, 2010	5	4.3
21	Collards	11,223[2]	Mustard Greens	46904509	October 15, 2010	5	4.3
22	Kale	3,994[2]	Mustard Greens	46904509	October 15, 2010	5	4.3
23	Kohlrabi	Not Listed	Cabbage, Broccoli, Cauliflower	46904509	October 15, 2010	5	4.3
24	Mizuna	Not Listed	Mustard Greens	46904509	October 15, 2010	5	4.3
25	Mustard greens	8,323[2]	Mustard Greens	46904509	October 15, 2010	5	4.3
26	Mustard spinach	Not Listed	Mustard Greens	46904509	October 15, 2010	5	4.3
27	Rape greens	Not Listed	Mustard Greens	46904509	October 15, 2010	5	4.3
28	Amaranth	939[4]	Head Lettuce, Leaf Lettuce, Spinach	46904508	October 15, 2010	4	4.4
29	Arugula	Not Listed	Head Lettuce, Leaf Lettuce, Spinach	46904508	October 15, 2010	4	4.4
30	Cardoon	Not Listed	Celery	46904508	October 15, 2010	4	4.4
31	Celery	29,600	Celery	46904508	October 15, 2010	4	4.4

Candidate No.	Crop Candidate	Bearing / Harvested Acres 2011/2012[1]	Residue Data to Support	MRID #	Date Registered	Crop Group No.	Document Section Number
32	Celtuce	Not Listed	Celery	46904508	October 15, 2010	4	4.4
33	Chervil	Not Listed	Head Lettuce, Leaf Lettuce, Spinach	46904508	October 15, 2010	4	4.4
34	Chinese celery	Not Listed	Celery	46904508	October 15, 2010	4	4.4
35	Chrysanthemum	Not Listed	Head Lettuce, Leaf Lettuce, Spinach	46904508	October 15, 2010	4	4.4
36	Corn salad	Not Listed	Head Lettuce, Leaf Lettuce, Spinach	46904508	October 15, 2010	4	4.4
37	Cress	Not Listed	Head Lettuce, Leaf Lettuce, Spinach	46904508	October 15, 2010	4	4.4
38	Dandelion	Not Listed	Head Lettuce, Leaf Lettuce, Spinach	46904508	October 15, 2010	4	4.4
39	Dock	Not Listed	Head Lettuce, Leaf Lettuce, Spinach	46904508	October 15, 2010	4	4.4
40	Endive (escarole)	5,170	Head Lettuce, Leaf Lettuce, Spinach	46904508	October 15, 2010	4	4.4
41	Florence fennel	Not Listed	Celery	46904508	October 15, 2010	4	4.4
42	Lettuce, Head and Leaf	177,300	Head Lettuce, Leaf Lettuce	46904508	October 15, 2010	4	4.4
43	Orach	Not Listed	Head Lettuce, Leaf Lettuce, Spinach	46904508	October 15, 2010	4	4.4
44	Parsley	4,240[2]	Head Lettuce, Leaf Lettuce, Spinach	46904508	October 15, 2010	4	4.4
45	Purslane	Not Listed	Head Lettuce, Leaf Lettuce, Spinach	46904508	October 15, 2010	4	4.4
46	Radicchio	Not Listed	Head Lettuce, Leaf Lettuce, Spinach	46904508	October 15, 2010	4	4.4
47	Rhubarb	1,404[2]	Celery	46904508	October 15, 2010	4	4.4
48	Spinach, Fresh and Processed	45,600	Spinach	46904508	October 15, 2010	4	4.4
49	Swiss chard	Not Listed	Celery	46904508	October 15, 2010	4	4.4
50	Globe Artichoke	7,800	Globe Artichoke	48697607	May 2, 2013	N/A	4.5
51	Pomegranate	24,517[2]	Pomegranate	48697606	May 2, 2013	N/A	4.6
52	Pineapple	10,211[2]	Pineapple	48697610	May 2, 2013	N/A	4.7
53	Coffee	6,100	Coffee	48697604	May 2, 2013	N/A	4.8

[1] USDA National Agricultural Statistics Service. http://www.nass.usda.gov

[2] USDA Census of Agriculture, 2007. http://www.agcensus.usda.gov

[3] Crop Profile for Rapini in California. http://www.ipmcenters.org/cropprofiles/docs/carapini.pdf

[4] USDA Census of Agriculture, 2002. http://www.agcensus.usda.gov

3.0 Product Introduction and Overview

3.1 – General Product Information

Spirotetramat, a spirocyclic tetramic acid derivative, is a unique foliar insecticide, developed exclusively by Bayer CropScience (2). The product has a new and unique mode of action classified as an Inhibitor of Acetyl CoA carboxylase or lipid biosynthesis inhibitor, IRAC Mode of Action Group 23 (3). Spirotetramat is an oral intoxicant and is active primarily on immature target insects. In addition to its control of immature life stages, spirotetramat also has a strong inhibitory effect on target insect reproduction; adult female insects lay significantly fewer eggs or live offspring and there is poor survivorship among the young that are produced. These factors contribute to extending the residual control of target pest populations.

Following application to plant foliage, spirotetramat moves through the leaf cuticle, converted to a weak acid, and is translocated primarily in the phloem and somewhat in the xylem throughout treated plants. Systemic movement is both basipetal and acropetal, thereby providing control of target pest insects feeding on plant foliage as well as on roots, including the suppression of nematodes. New foliage and root growth that occurs after the application of spirotetramat is also protected (4). In worldwide biological development trials, spirotetramat has proven to be highly efficacious against aphids, mealybugs, psyllids, scales, certain thrips species, and whiteflies (5,6).

3.2 – Human and Environmental Safety

Spirotetramat is a reduced risk compound. The toxicological findings of the Health Effects Division for technical spirotetramat are:

- Low acute toxicity via the oral, dermal (Toxicity Category III) and inhalation (Toxicity Category IV) routes of exposure.
- Nonirritating to the skin (Toxicity Category IV).
- Irritant to the eyes (Toxicity Category II).
- Exhibits a dermal sensitization potential in animals and humans.
- No evidence of tumor formation was found following long-term studies of rodents, and spirotetramat was also negative for mutagenicity and clastogenicity in several standard *in vivo* and *in vitro* assays.
- No significant developmental or reproductive effects.
- Not neurotoxic.
- Classified as not likely to be carcinogenic to humans.

Based on the human and environmental safety data submitted, EPA has expressly confirmed that "[s]pirotetramat overall presents a significantly lower risk to humans and the environment compared to alternatives registered for the same use patterns."[1] This conclusion alone warrants EPA's approval of the minor uses identified in this petition as supporting an extension of the exclusive use period, and granting the requested three-year extension of the exclusive use period for spirotetramat.

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[1] EPA, Memorandum from L. Rossi, Director, Registration Division, to Steven Bradbury, Director, **Office of Pesticide Programs, Re: Consideration of Registration for the New Chemical Spirotetramat** (Oct. 15, 2010) at 24 (available at: http://www.regulations.gov/#!documentDetail;D=EPA-HQ-OPP-2010-0130-0079).

The data for the alternative products within this document were obtained from a number of sources including EPA Reregistration Eligibility Decisions, the USDA/ARS Pesticide Properties Database, The Pesticide Manual (12th edition), European Union and UK monographs, Canadian PMRA and the National Registration Authority of Australia. The data were selected with priority given to available EPA and USDA data, with other sources used to supply missing elements. The data for spirotetramat were obtained from registration studies submitted to EPA.

3.3 – Resistance Management Considerations

The prolific reproductive capacity of insects and repeated use of a limited selection of chemical insecticides/modes of action are key factors for the development of insecticide resistance. Growers, especially those of minor-use crops, must have an array of pest control options available to them and those options must be used wisely to maintain their effectiveness for as long as possible; in this light, Bayer CropScience has developed very specific recommendations relative to the use of spirotetramat in both annual and perennial crops (7, 8, 9). Spirotetramat provides a unique mode of action and is a very effective alternative in orchard and vegetable crops where organophosphate, pyrethroid, and neonicotinoid chemistries have historically dominated. In addition, in many pest segments such as aphids, mealybugs, scales, and thrips, spirotetramat **is the only insecticide registered for these pests on both annual and perennial crops within IRAC Mode of Action Group 23**.

Laboratory investigations were conducted with spirotetramat against several sucking pest species using strains resistant and susceptible to conventional insecticides, including organophosphates, carbamates, pyrethroids, chlorinated hydrocarbons and neonicotinoids. Species tested included green peach aphid (*Myzus persicae*), cotton aphid (*Aphis gossypii*), damson hop aphid (*Phorodon humuli*), cotton whitefly (*Bemisia tabaci*) and greenhouse whitefly (*Trialeurodes vaporariorum*). More thorough investigations were conducted with spirotetramat against biochemically characterized, multi-resistant strains of *Bemisia tabaci* derived from vegetables from different parts in the world, including southern Spain. The results revealed spirotetramat to be highly active on both insecticide-susceptible and resistant strains of several sucking pest species and showed no cross-resistance to other chemical classes of insecticides tested.

Spirotetramat can be used in alternation/rotation with any insecticide of other mode of action classes. Bayer CropScience strongly encourages that spirotetramat be utilized in a block or window approach where chemical classes having a different mode of action are utilized in rotational sequences. Using a block rotation or windowed approach, along with other sound IPM practices, is considered an effective use strategy for preventing or delaying an insect pest's ability to develop resistance to a given class of chemistry. While providing growers with excellent control of target pests, spirotetramat also plays a key role in resistance management strategies to help preserve existing chemical classes in the market.

3.4 – Contribution to IPM Systems

The USDA has defined Integrated Pest Management (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". Spirotetramat has an excellent fit as a chemical component in IPM programs for agricultural pests.

Spirotetramat has minimal effects on beneficial insects when applied according to the product label. In internal trials, Bayer CropScience has determined spirotetramat to be non-toxic or only slightly harmful (categories I and II, IOBC classification) to four species of parasitoids and fifteen species of predatory Coleoptera, Hemiptera, predatory mites and spiders. Moderately harmful to harmful effects (categories III and IV, IOBC classification) were found for three species of predatory mites only.

Spirotetramat has suppressive activity on pest spider mites as well and both internal and external field trials have demonstrated that predatory mite and pest spider mite population ratios remain constant following application of spirotetramat. Additional laboratory and field testing have shown very low impact on beneficial predators and parasites, both native and introduced species, such as coccinellids, chrysopids, and spiders(10, 11). Excellent product efficacy and preservation of beneficial organisms combine to offer a high level of sustained pest control that significantly reduces the need for follow-up insecticide treatments, making spirotetramat an ideal fit in IPM programs on both major and minor-use crops (12).

Spirotetramat will further support IPM objectives by contributing to reduced pesticide loads in the environment. Spirotetramat is a selective insecticide with excellent residual control and low single and seasonal application rates. Its systemic property permits control of pests hidden in dense crop canopies, thereby reducing the potential for pest resurgence and re-treatment due to insufficient spray coverage. Spirotetramat has claimed treated acres once occupied by older chemistries that are less selective and that pose greater risk to human health, wildlife and the environment.

Spirotetramat should be considered an ideal product selection when beneficials can no longer maintain insect pest populations below economic thresholds and treatment is warranted. With its low effects on beneficials, spirotetramat allows these organisms to continually manage damaging pests once population densities have been effectively reduced, promoting a true IPM program.

4.0 Minor-Use Crop Specific Discussions

4.1 - Citrus Fruits: Grapefruit, Lemon, Lime, Key lime, Kumquat, Pummelo, Tangerine, Tangelo, and Satsuma

These nine minor-use citrus crops are often included in the broad general crop terminology "citrus" within literature and publications, covering many different citrus types. Other members are contained in the term "citrus" however virtually no published information exists on those members for inclusion in this section due to their very small acreage relative to other members.

Key pests plaguing both major and minor citrus crops for which spirotetramat is labeled include Asian citrus psyllid, citrus thrips, California red scale, and aphids. Table 2 provides a summary of the major alternative insecticides presently registered for control of these citrus pests. Each of the alternative products listed in Table 2, arranged in order of percent market share from high to low, account for more than 5% of the foliar treated acres.

Table 2. Alternatives to Spirotetramat for Use on Citrus Fruits: Grapefruit, Lemon, Lime, Key lime, Kumquat, Pummelo, Tangerine, Tangelo, and Satsuma.

Active Ingredient	Brand	IRAC Group	Mode of Action
SPIROTETRAMAT	**MOVENTO**	**23**	**Inhibitor of Acetyl CoA carboxylase**
ABAMECTIN	AGRI-MEK	6	Chloride channel activator
ZETA-CYPERMETHRIN	MUSTANG	3	Sodium channel modulator
IMIDACLOPRID	ADMIRE	4A	Nicotinic acetylcholine receptor agonist
FENPROPATHRIN	DANITOL	3	Sodium channel modulator
CHLORPYRIFOS	LORSBAN	1B	Acetylcholinesterase inhibitor
SPINETORAM	DELEGATE	5	Nicotinic acetylcholine receptor allosteric activator
DIMETHOATE	DIMETHOATE	1B	Acetylcholinesterase inhibitor

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

Alternatives Pose Greater Risk to Human Health

Acute toxicity evaluations of the spirotetramat end-use product MOVENTO® and alternative end-use insecticides are summarized in Table 3 with additional comments below.

Table 3. Comparison of the Toxicity Categories and Signal Words of Spirotetramat End-Use Products with Alternative End-Use Insecticides for Use on Citrus Fruits: Grapefruit, Lemon, Lime, Key lime, Kumquat, Pummelo, Tangerine, Tangelo, and Satsuma.

Active Ingredient	Brand	Toxicity Category	Signal Word
Spirotetramat	**MOVENTO®**	III	Caution
Abamectin	Agri-Mek® 0.15 EC	II	Warning
Chlorpyrifos	Lorsban® 50W	I	Danger
Dimethoate	Dimethoate 4 EC	I	Danger
Fenpropathrin	Danitol®	I	Danger
Imidacloprid	Admire® Pro	III	Caution
Spinetoram	Delegate®	III	Caution
Zeta-cypermethrin	Mustang®	II	Warning

The spirotetramat end-use product MOVENTO® carries the signal word "Caution" (Category III) based on oral, dermal, and eye irritation hazards. The formulation demonstrates low toxicity by the oral, dermal, and inhalation routes of exposure. Of the seven end-use products being compared to spirotetramat in this section, three products have a Category I (Danger) classification, two products have a Category II (Warning) classification, and two products have a Category III (Caution) classification. Therefore, five of the seven alternative products carry more hazardous acute toxicity classifications than the spirotetramat end-use product.

Toxicity evaluations of spirotetramat and alternative insecticides are summarized in Table 4 with additional comments below.

Table 4. Active Ingredient Toxicology Summary for Spirotetramat and Major Alternative Insecticides for Use on Citrus Fruits: Grapefruit, Lemon, Lime, Key lime, Kumquat, Pummelo, Tangerine, Tangelo, and Satsuma.

Active Ingredient	Acute Toxicity	Geno-toxicity	Reproductive Toxicity (Primary Evidence)	Develop-mental Toxicity (Primary Evidence)	Onco-genicity Class [d]	Chronic Ref Dose (mg/kg/day)
Spirotetramat	**Warning**	–[a]	–	–	**E**	**0.132**
Abamectin	Danger		+[c]	–	E	0.00012
Chlorpyrifos	Warning	–	–	–	E	0.0003
Dimethoate	Danger	+/-[b]	–	–	C	0.0005

Active Ingredient	Acute Toxicity	Geno-toxicity	Reproductive Toxicity (Primary Evidence)	Develop-mental Toxicity (Primary Evidence)	Onco-genicity Class [d]	Chronic Ref Dose (mg/kg/day)
Fenpropathrin	Danger	–	–	–	E	0.025
Imidacloprid	Warning	+/-	–	–	E	0.057
Spinetoram	Caution	–	–	–	E	0.0249
Zeta-cypermethrin	Warning	-	–	–	C	0.06

[a] "-" indicates no evidence within a particular category
[b] "+/-" indicates positive and negative findings were observed
[c] "+" indicates positive findings within a category
[d] E: not likely; C: possible; S: suggestive; B2: probable

Spirotetramat, registered by EPA on October 15, 2010, is a new, safer chemistry that replaces organophosphates, neonicotinoids, pyrethroids and other chemistries because of its unique systemicity and broad pest spectrum in both major and minor-use crops. Spirotetramat showed no evidence of oncogenicity in any of the studies conducted in the rat and mouse and is therefore, classified as *not likely to be carcinogenic to humans (Class E).* Two of the alternative products (dimethoate and zeta-cypermethrin) are classified as *possible human carcinogens* (Class C). The remaining products are classified as *not likely to be carcinogenic in humans* (Class E).

The reproductive and prenatal developmental toxicity studies in rats and rabbits provided no evidence to suggest that spirotetramat nor the alternative products possesses either a teratogenic or primary toxicological potential, as non-maternal toxicity was identified at equivalent or higher doses than maternal toxicity in both species. Finally, the parental, reproductive, and offspring NOAELs (mg/kg/day) of many of the comparative products are, in general, significantly lower than the male (M) / female (F) parental, reproductive, and offspring NOAELs determined for spirotetramat.

Based on specific neurotoxicity screening assessments conducted acutely in the rat and incorporated as a satellite investigation as part of the 1-year chronic rat study, spirotetramat did not provide any qualitative or quantitative evidence of a neurotoxic potential. In addition to the specific neurotoxicity testing, no treatment-related clinical signs, changes in absolute brain weight, neuropathological, or neurobehavioral findings were noted in the general toxicity studies (i.e. acute, subacute, subchronic, developmental, reproduction, and chronic). Of the products being compared to spirotetramat in this section, two of the actives, unlike spirotetramat, have cholinesterase inhibiting properties (chlorpyrifos and dimethoate) and three actives showed evidence of inducing neurological toxicity (chlorpyrifos, dimethoate, and imidacloprid).

In vivo and *in vitro* mutagenicity studies with spirotetramat and its metabolites indicate that spirotetramat is not mutagenic. Of the products being compared to spirotetramat in this section, two actives (dimethoate and imidacloprid) showed some evidence of positive responses (*in vivo* and/or *in vitro*) in gene mutational testing or cytogenetic testing.

These findings suggest an overall favorable toxicology package for spirotetramat compared to the alternative products used in these minor-use citrus crops.

Alternatives Pose Greater Risk to the Environment

Risk assessments demonstrate that spirotetramat 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 5 is a comparison based on Tier 1 risk quotients taken from the reduced risk submissions in which quantitative values of these risk quotients are provided.

Table 5. Summary of Ecological Risk for Spirotetramat and Major Alternative Products for Use on Citrus Fruits: Grapefruit, Lemon, Lime, Key lime, Kumquat, Pummelo, Tangerine, Tangelo, and Satsuma.

Chemical	Avian Acute	Avian Chronic	Mammal Acute	Mammal Chronic	Fish Acute	Fish Chronic	Daphnia Acute	Daphnia Chronic	Marine Acute	Bees[1]
Spirotetramat	0.01	2.43	0.02	0.45	<0.01	<0.01	<0.01	<0.01	<0.01	>100
Abamectin	0.02	>0.12	0.30	12.93	0.02	3.23	0.18	1.00	0.29	0.41[2]
Chlorpyrifos	9.59	52.15	5.83	1131.11	26.76	18.90	481.67	609.60	1376.20	0.059[2]
Dimethoate	0.12	30.00	0.29	69.41	<0.01	<0.01	<0.01	0.05	<0.01	0.16
Fenpropathrin	0.02	7.8	1.8	3.3	0.71	4.8	2.9	4.5	74	0.05
Imidacloprid	0.07	2.32	0.11	2.63	<0.01	<0.01	<0.01	<0.01	0.17	0.04
Spinetoram	< 0.02	0.38	0.01	0.06	<0.01	<0.01	<0.01	4.5	<0.01	0.0029
Zeta-cypermethrin	0.01	1.14	0.10	4.12	0.44	1.86	1.38	288.89	76.60	0.023

No Tier 1 LOC exceedances, or for honey bees, practically non-toxic

Between the endangered species LOC and the high risk LOC for acute risk. Between 1 and 5 times the LOC for chronic risk or for honey bees, moderately toxic.

Greater than the high risk LOC for acute risk. Greater than 5X the LOC for chronic risk. Highly toxic to honey bees.

[1]The "Bees" column gives the 48 h contact LD50 value since there is no EPA risk paradigm for bees with the color indicative of the hazard classification as noted above.

[2] Toxicity after 24 hours

On an acre for acre replacement, the use of spirotetramat reduces the amount of active ingredient applied when compared to most alternative products. Of the seven alternative products discussed in this section, dimethoate and imidacloprid are applied at similar rates. Most notable among the alternative insecticide groups, the organophosphate insecticides have 5 times or higher seasonal application rates than spirotetramat.

In addition to low application rates, spirotetramat can reduce the environmental burden associated with retreatment of resurgent pest populations. This is possible because of two other unique properties of spirotetramat: (1) systemic movement allows control of target pest infestations hidden in dense crop canopies and (2) reduced fecundity of adult female target insects extends residual control into the next pest generation.

The estimated ground water concentration for spirotetramat is negligible (i.e., consumes zero percent of the cPAD). This is true even after considering the combined residues of spirotetramat and its degradates. Spirotetramat degrades rapidly in soil and water, leading to low estimated concentrations in aquatic environments. Human exposure to spirotetramat residues in water is anticipated to be negligible, consuming 0% of the cPAD for all population subgroups. By comparison, estimated drinking water concentrations consume most or all of the cPAD for many of the alternatives.

Therefore, among the alternative compounds, only spirotetramat is expected to have low surface water, as well as low ground water contamination risks.

Spirotetramat has minimal acute, adult risk to bees (LD_{50} >100 µg a.i./bee; practically non-toxic). For citrus, spirotetramat compares very favorably to alternative products and is the least toxic insecticide to honeybees, characterized as "practically non-toxic" to honey bees. Conversely, all of the alternative insecticides are characterized as "highly toxic" to bees (contact LD_{50} <1 µg/bee).

Bayer CropScience has conducted a comprehensive honey bee safety research and evaluation program with spirotetramat. Field studies designed to evaluate safety to bees following a field exposure to spirotetramat at bloom have been conducted in *Phacelia*, melon and citrus. There were no adverse effects to bees or colony health noted in these studies.

These findings suggest an overall favorable environmental package for spirotetramat compared to the alternative products used in these minor-use citrus crops.

4.1.2 – FIFRA Criterion III: The minor use pesticide plays or will play a significant part in managing pest resistance

In the fight against Asian citrus psyllid and the devastating bacterial disease that it vectors (Huanglongbing or citrus greening), Florida citrus growers may apply up to 12 or more foliar sprays of various products per year. Since 2005, Florida citrus growers have extensively utilized organophosphate (IRAC Group 1B), neonicotinoid (IRAC Group 4) and pyrethroid (IRAC Group 3) chemistries due to their high level of efficacy. Additional modes of action having activity against Asian citrus psyllid are from IRAC Groups 5 and 6, thus the number of available modes of action is somewhat limited, as evidenced in Table 2 above. Due to the limited availability of modes of action, very little rotation has occurred over the years and has led to Asian citrus psyllid becoming more tolerant to these classes, particularly the neonicotinoid and pyrethroid chemistries, as evidenced in laboratory bioassay studies (35). Spirotetramat, having a different mode of action and classified as an IRAC Group 23 product, registered on both major and minor members of the citrus crop grouping, serves as a highly effective tool for rotational purposes to help preserve the efficacy of existing products.

A similar situation is present in California citrus, albeit with different pests, California red scale and citrus thrips. For California red scale, California growers have experienced limited availability of effective products having different modes of action and resistance has developed to organophosphates (chlorpyrifos, methidathion) and carbamate (carbaryl) chemical classes which share a common mode of action (36). As a result, heavy reliance on a juvenile hormone mimic (pyriproxyfen) has occurred, increasing the selection pressure on this mode of action and observations indicate that resistance may be developing (32). For citrus thrips, this pest has a history of rapidly developing resistance to crop protection products, particularly when the same mode of action is used repeatedly. Over the years, resistance has developed to organophosphates (dimethoate), carbamates (formetanate hydrochloride), and pyrethroids (beta-cyfluthrin, fenpropathrin) (37,38). The addition of spirotetramat, with its alternative mode of action, serves as another effective tool for California citrus growers to utilize in the control of California red scale and citrus thrips.

4.1.3 - FIFRA Criterion IV: The minor use pesticide plays or will play a significant part in an integrated pest management program

All citrus types, both major and minor, and all geographical production areas are plagued in varying degrees by destructive insect infestations (22, 23, 24, 25, 26) – the most feared being Asian citrus psyllid, the vector of the bacterial disease Huanglongbing (HLB) or citrus greening. Testing conducted with spirotetramat by Bayer CropScience and university scientists has shown high levels of efficacy

against Asian citrus psyllid (13,14,15), as well as additional key pests such as citrus thrips (16), California red scale (17, 18), and aphids (19). In addition to providing direct control of these destructive pests of citrus, studies have shown spirotetramat to have minimal impact on beneficial predators and parasitoids in general (10,11) and those more common to citrus specifically (20,21). The combination of high efficacy and minimal impact on beneficial predators and parasitoids found in citrus production which promotes true IPM strategies has resulted in numerous state and university recommendations for spirotetramat (27, 28, 29, 30, 31, 32, 33), as well as a plea made by the industry when the threat of losing spirotetramat arose in 2010 (34) .

4.2 Dry Bulb Onion

The key pest plaguing dry bulb onion is onion thrips. Table 6 provides a summary of the major alternative insecticides presently registered for control of onion thrips. Each of the alternative products listed in Table 6, arranged in order of percent market share from high to low, account for more than 5% of the foliar treated acres.

Table 6. Alternatives to Spirotetramat for Use on Dry Bulb Onion

Active Ingredient	Brand	IRAC Group	Mode of Action
SPIROTETRAMAT	**MOVENTO**	**23**	**Inhibitor of Acetyl CoA carboxylase**
METHOMYL	LANNATE	1A	Acetylcholinesterase inhibitor
LAMBDA-CYHALOTHRIN	WARRIOR	3	Sodium channel modulator
SPINETORAM	RADIANT	5	Nicotinic acetylcholine receptor allosteric activator
OXAMYL	VYDATE	1A	Acetylcholinesterase inhibitor
CHLORPYRIFOS	LORSBAN	1B	Acetylcholinesterase inhibitor
ZETA-CYPERMETHRIN	MUSTANG	3	Sodium channel modulator

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

Alternatives Pose Greater Risk to Human Health

Acute toxicity evaluations of the spirotetramat end-use product MOVENTO® and alternative end-use insecticides are summarized in Table 7 with additional comments below.

Table 7. Comparison of the Toxicity Categories and Signal Words of Spirotetramat End-Use Products with Alternative End-Use Insecticides for Use on Dry Bulb Onion.

Active Ingredient	Trade Name	Toxicity Category	Signal Word
Spirotetramat	**MOVENTO®**	III	Caution
Chlorpyrifos	Lorsban® 50W	I	Danger
Lambda-Cyhalothrin	Warrior®	II	Warning
Methomyl	Lannate®	I	Danger
Oxamyl	Vydate® L	I	Danger
Spinetoram	Radiant®	III	Caution
Zeta-cypermethrin	Mustang®	II	Warning

The spirotetramat end-use product MOVENTO® carries the signal word "Caution" (Category III) based on oral, dermal, and eye irritation hazards. This formulation demonstrates low toxicity by the oral, dermal, and inhalation routes of exposure. Of the six end-use products being compared to spirotetramat in this section, three products have a Category I (Danger) classification, two products have a Category II (Warning) classification, and one product has a Category III (Caution) classification. Therefore, five of the six alternative products carry more hazardous acute toxicity classifications than the spirotetramat end-use product MOVENTO®.

Toxicity evaluations of spirotetramat and alternative insecticides are summarized in Table 8 with additional comments below.

Table 8. Active Ingredient Toxicology Summary for Spirotetramat and Major Alternative Insecticides for Use on Dry Bulb Onion.

Chemical (Technical)	Acute Toxicity	Geno-toxicity	Repro-ductive Toxicity (Primary Evidence)	Develop-mental Toxicity (Primary Evidence)	Onco-genicity Class[c]	Q_1^* (mg/kg/day)$^{-1}$	Chronic Ref Dose (mg/kg/day)
Spirotetramat	**Warning**	–[a]	–	–	**E**	–	**0.132**
Chlorpyrifos	Warning	–	–	–	E	–	0.0003
Lambda-Cyhalothrin	Warning	–	–	–	E	–	0.001
Methomyl	Danger	–	–	–	E	–	0.008
Oxamyl	Danger	–	–	+[b]	E	–	0.025
Spinetoram	Caution	–	–	–	E	–	0.0249
Zeta-cypermethrin	Warning	+[d]	–	–	C		0.06

[a] "-" indicates no evidence within a particular category
[b] "+" indicates positive findings within a category
[c] E: not likely; C: possible; S: suggestive; B2: probable
[d] Weak evidence for genotoxicity

Spirotetramat, registered by EPA on October 15, 2010, is a new, safer chemistry that will replace organophosphates, neonicotinoids, pyrethroids and other chemistries because of its unique systemicity and broad pest spectrum. Spirotetramat showed no evidence of oncogenicity in any of the studies conducted in the rat and mouse and is therefore, classified as *not likely to be carcinogenic to humans (Class E)*. One of the alternative products, zeta-cypermethrin, is classified as a *possible human carcinogen* (Class C); the remaining products are classified as *not likely to be carcinogenic in humans* (Class E).

The reproductive and prenatal developmental toxicity studies in rats and rabbits provided no evidence to suggest that spirotetramat possesses either a teratogenic or primary toxicological potential, as non-maternal toxicity was identified at equivalent or higher doses than maternal toxicity in both species. The parental, reproductive, and offspring NOAELs (mg/kg/day) of many of the comparative products are, in general, significantly lower than the male (M) / female (F) parental, reproductive, and offspring NOAELs determined for spirotetramat.

Based on specific neurotoxicity screening assessments conducted acutely in the rat and incorporated as a satellite investigation as part of the 1-year chronic rat study, spirotetramat did not provide any qualitative or quantitative evidence of a neurotoxic potential. In addition to the specific neurotoxicity testing, no treatment-related clinical signs, changes in absolute brain weight, neuropathological, or neurobehavioral findings were noted in the general toxicity studies (i.e. acute, subacute, subchronic,

developmental, reproduction, and chronic). Of the products being compared to spirotetramat in this section, three of the actives, unlike spirotetramat, have cholinesterase inhibiting properties (chlorpyrifos, methomyl, and oxamyl) and one active showed evidence of inducing neurological toxicity (chlorpyrifos).

In vivo and *in vitro* mutagenicity studies with spirotetramat and its metabolites indicate that spirotetramat is not mutagenic. Of the products being compared to spirotetramat in this section, one actives (zeta-cypermethrin) showed some evidence of positive responses (*in vivo* and/or *in vitro*) in gene mutational testing or cytogenetic testing.

These findings suggest an overall favorable toxicology package for spirotetramat compared to the alternative products used in minor-use dry bulb onion.

Alternatives Pose Greater Risk to the Environment

Risk assessments demonstrate that spirotetramat 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 9 is a comparison of spirotetramat and alternative products based on Tier 1 risk quotients taken from the reduced risk submissions in which quantitative values of these risk quotients are provided.

Table 9. Summary of Ecological Risk for Spirotetramat and Major Alternative Products for Use on Dry Bulb Onion.

Chemical	Avian Acute	Avian Chronic	Mammal Acute	Mammal Chronic	Fish Acute	Fish Chronic	Daphnia Acute	Daphnia Chronic	Marine Acute	Bees[1]
Spirotetramat	**0.01**	**2.43**	**0.02**	**0.45**	**<0.01**	**<0.01**	**<0.01**	**<0.01**	**<0.01**	**>100**
Chlorpyrifos	9.59	52.15	5.83	1131.11	26.76	18.90	481.67	609.60	1376.20	0.059[3]
Lambda- Cyhalothrin	0.42	179.57	6.96	29.93	64.0	208.0	55.56	135000	1020.0	0.038
Methomyl	0.39	4.76	21.20	9.52	0.26	1.95	14.77	205	5.21	<0.5
Oxamyl	4.10	139.29	241.69	24.17	0.01	0.02	0.06	0.01	<0.01	0.31
Spinetoram	< 0.02	0.38	0.01	0.06	<0.01	<0.01	<0.01	4.5	<0.01	0.0029
Zeta-cypermethrin	0.01	1.14	0.10	4.12	0.44	1.86	1.38	288.89	76.60	0.023

No Tier 1 LOC exceedances, or for honey bees, practically non-toxic

Between the endangered species LOC and the high risk LOC for acute risk. Between 1 and 5 times the LOC for chronic risk or for honey bees, moderately toxic.

Greater than the high risk LOC for acute risk. Greater than 5X the LOC for chronic risk. Highly toxic to honey bees.

[1]The "Bees" column gives the 48 h contact LD50 value since there is no EPA risk paradigm for bees with the color indicative of the hazard classification as noted above.
[2] NA = Not available
[3] Toxicity after 24 hours

On an acre for acre replacement, the use of spirotetramat reduces the amount of active ingredient applied when compared to most alternative products. Of the six alternative products discussed in this section, only spinetoram is applied at similar rates; the organophosphate and carbamate insecticide alternatives have much higher seasonal application rates than spirotetramat.

In addition to low application rates, spirotetramat can reduce the environmental burden associated with retreatment of resurgent pest populations. This is possible because of spirotetramat's ability to reduce fecundity of adult female insects which extends residual control into the next pest generation.

The estimated ground water concentration for spirotetramat is negligible (i.e., consumes zero percent of the cPAD). This is true even after considering the combined residues of spirotetramat and its degradates. Spirotetramat degrades rapidly in soil and water, leading to low estimated concentrations in aquatic environments. Human exposure to spirotetramat residues in water is anticipated to be negligible consuming 0% of the cPAD for all population subgroups. By comparison, estimated drinking water concentrations consume most or all of the cPAD for many of the alternatives. Therefore, among the alternative compounds, only spirotetramat is expected to have low surface water as well as low ground water contamination risks.

Spirotetramat has minimal acute, adult risk to bees (LD_{50} >100 µg a.i./bee; practically non-toxic). For dry bulb onion, spirotetramat compares very favorably to alternative products and is the least toxic insecticide to honeybees, characterized as "practically non-toxic" to honey bees. All of the alternative insecticides are characterized as "highly toxic" to bees (contact LD_{50} <1 µg/bee).

Bayer CropScience has conducted a comprehensive honey bee safety research and evaluation program. Field studies designed to evaluate safety to bees following a field exposure to spirotetramat at bloom have been conducted in *Phacelia*, melon and citrus. There were no adverse effects to bees or colony health noted in these studies.

These findings suggest an overall favorable environmental package for spirotetramat compared to the alternative products used in dry bulb onion.

4.2.2 – FIFRA Criterion III: The minor use pesticide plays or will play a significant part in managing pest resistance

Onion thrips, the vector of Iris Yellow Spot Virus in onion, have a relatively high propensity to develop resistance to various chemical classes if sound resistance management practices are not employed by end users. On a global level, onion thrips have developed resistance to several pyrethroids, organophosphates, carbamates, and members of other chemical classes (39). As seen in Table 6, there are two active ingredients from IRAC Group 1A, one from Group 1B, two from Group 3, and one from Group 5 – in short, a very limited number of different modes of action available to end users. In order to maintain susceptibility in onion thrips to all available chemical tools, university researchers recommend "blocks" or "windows" where alternations of chemical classes are made throughout the growing season; this was the justification used by various onion-producing states for the numerous Section 18's granted prior to Section 3 registration. Spirotetramat has shown excellent control of onion thrips alone (40,41), as well as when a component of a rotational mode of action program(42) ; spirotetramat is one of the recommended compounds in this rotational scheme due to its excellent residual efficacy against this pest (43,44).

4.2.3 - FIFRA Criterion IV: The minor use pesticide plays or will play a significant part in an integrated pest management program

Predators can exert a reduction in the onion thrips population but densities are not sufficient until late in the summer after considerable damage has occurred. Predators can include black hunter thrips, big-eyed bug, minute pirate bug, and green lacewing larvae (45). In order to preserve building populations of these beneficial predators of onion thrips, it is necessary to utilize chemical tools with low impact on these beneficial arthropods. As indicated earlier in this document, spirotetramat has shown low impact on many of these species (10,11,12), allowing for true IPM to be practiced in the management of onion thrips.

4.3 - Brassica (Cole) Leafy Vegetables: Broccoli, Broccoli raab (rapini), Brussels sprouts, Cabbage, Cauliflower, Cavalo broccolo, Chinese broccoli (gai lon), Chinese cabbage (bok choy), Chinese cabbage (napa), Chinese mustard cabbage (gai choy), Collards, Kale, Kohlrabi, Mizuna, Mustard greens, Mustard spinach, and Rape Greens

Many members of the Brassica (Cole) Leafy Vegetable crop grouping are extremely minor in acreage, to the point where no specific recommendations or other information exists for which to cite in this section. However, the key pests infesting all members of the Brassica (Cole) Leafy Vegetable crop grouping are various species of aphids. Table 10 provides a summary of the major alternative insecticides presently registered for control of aphids in these minor-use crops. Each of the alternative products listed in Table 10, arranged in order of percent market share from high to low, account for more than 5% of the foliar treated acres.

Table 10. Alternatives to Spirotetramat for Use on Brassica (Cole) Leafy Vegetables: Broccoli, Broccoli raab (rapini), Brussels sprouts, Cabbage, Cauliflower, Cavalo broccolo, Chinese broccoli (gai lon), Chinese cabbage (bok choy), Chinese cabbage (napa), Chinese mustard cabbage (gai choy), Collards, Kale, Kohlrabi, Mizuna, Mustard greens, Mustard spinach, and Rape Greens.

Active Ingredient	Brand	IRAC Group	Mode of Action
SPIROTETRAMAT	**MOVENTO**	**23**	**Inhibitor of Acetyl CoA carboxylase**
IMIDACLOPRID	ADMIRE PRO	4A	Nicotinic acetylcholine receptor agonist
DIMETHOATE	DIMETHOATE	1B	Acetylcholinesterase inhibitor
BETA-CYFLUTHRIN & IMIDACLOPRID	LEVERAGE 360	3, 4A	Sodium channel modulator; Nicotinic acetylcholine receptor agonist
MALATHION	MALATHION	1B	Acetylcholinesterase inhibitor
OXYDEMETON-METHYL	MSR	1B	Acetylcholinesterase inhibitor
THIAMETHOXAM	PLATINUM	4A	Nicotinic acetylcholine receptor agonist
LAMBDA-CYHALOTHRIN	WARRIOR	3	Sodium channel modulator

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

Alternatives Pose Greater Risk to Human Health

Acute toxicity evaluations of the spirotetramat end-use product MOVENTO® and alternative end-use insecticides are summarized in Table 11 with additional comments below.

Table 11. Comparison of the Toxicity Categories and Signal Words of Spirotetramat End-Use Products with Alternative End-Use Insecticides for Use on Brassica (Cole) Leafy Vegetables: Broccoli, Broccoli raab (rapini), Brussels sprouts, Cabbage, Cauliflower, Cavalo broccolo, Chinese broccoli (gai lon), Chinese cabbage (bok choy), Chinese cabbage (napa), Chinese mustard cabbage (gai choy), Collards, Kale, Kohlrabi, Mizuna, Mustard greens, Mustard spinach, and Rape Greens

Active Ingredient	Trade Name	Toxicity Category	Signal Word
Spirotetramat	**MOVENTO®**	III	Caution

Active Ingredient	Trade Name	Toxicity Category	Signal Word
Beta-cyfluthrin+Imidacloprid	Leverage® 360	III	Caution
Dimethoate	Dimethoate 4 EC	I	Danger
Imidacloprid	Admire® Pro	III	Caution
Lambda-Cyhalothrin	Warrior®	II	Warning
Malathion	Malathion 5 EC	II	Warning
Oxydemeton-methyl	MSR® Spray Concentrate	II	Warning
Thiamethoxam	Platinum®	III	Caution

The spirotetramat end-use product MOVENTO® carries the signal word "Caution" (Category III) based on oral, dermal, and eye irritation hazards. This formulation demonstrates low toxicity by the oral, dermal, and inhalation routes of exposure. Of the seven end-use products being compared to spirotetramat in this section, one product has a Category I (Danger) classification, three products have a Category II (Warning) classification, and three products have a Category III (Caution) classification. Therefore, four of the seven alternative products carry more hazardous acute toxicity classifications than the spirotetramat end-use product MOVENTO®.

Toxicity evaluations of spirotetramat and alternative insecticides are summarized in Table 12 with additional comments below.

Table 12. Active Ingredient Toxicology Summary for Spirotetramat and Major Alternative Insecticides for Use on Brassica (Cole) Leafy Vegetables: Broccoli, Broccoli raab (rapini), Brussels sprouts, Cabbage, Cauliflower, Cavalo broccolo, Chinese broccoli (gai lon), Chinese cabbage (bok choy), Chinese cabbage (napa), Chinese mustard cabbage (gai choy), Collards, Kale, Kohlrabi, Mizuna, Mustard greens, Mustard spinach, and Rape Greens.

Chemical (Technical)	Acute Toxicity	Geno-toxicity	Repro-ductive Toxicity (Primary Evidence)	Develop-mental Toxicity (Primary Evidence)	Onco-genicity Class [d]	Q_1* (mg/kg/day)$^{-1}$	Chronic Ref Dose (mg/kg/day)
Spirotetramat	**Warning**	–[a]	–	–	E	–	**0.132**
Beta-Cyfluthrin	Danger	–	–	–	E	–	0.024
Dimethoate	Danger	+/-[b]	–	–	C	–	0.0005
Imidacloprid	Warning	+/-	–	–	E	–	0.057
Lambda-Cyhalothrin	Warning	–	–	–	E	–	0.001
Malathion	Warning	+[e]	–	–	S		0.07
Oxydemeton-methyl	Danger	+/-	–	–	E	–	0.0005
Thiamethoxam	Caution	–	–	–	C	3.77	0.0006

[a] "-" indicates no evidence within a particular category
[b] "+/-" indicates positive and negative findings were observed
[c] "+" indicates positive findings within a category
[d] E: not likely; C: possible; S: suggestive; B2: probable
[e] Weak evidence for genotoxicity

Spirotetramat, registered by EPA on October 15, 2010, is a new, safer chemistry that will replace organophosphates, neonicotinoids, pyrethroids and other chemistries because of its unique systemicity

and broad pest spectrum. Spirotetramat showed no evidence of oncogenicity in any of the studies conducted in the rat and mouse and is therefore, classified as *not likely to be carcinogenic to humans (Class E)*. Two of the alternative products (dimethoate and thiamethoxam) are classified as *possible human carcinogens* (Class C) and one (malathion) as *suggestive evidence of carcinogenic potential* (Class S). The remaining products are classified as *not likely to be carcinogenic in humans* (Class E).

The reproductive and prenatal developmental toxicity studies in rats and rabbits provided no evidence to suggest that spirotetramat possesses either a teratogenic or primary toxicological potential, as non-maternal toxicity was identified at equivalent or higher doses than maternal toxicity in both species. The parental, reproductive, and offspring NOAELs (mg/kg/day) of many of the comparative products are, in general, significantly lower than the male (M) / female (F) parental, reproductive, and offspring NOAELs determined for spirotetramat.

Based on specific neurotoxicity screening assessments conducted acutely in the rat and incorporated as a satellite investigation as part of the 1-year chronic rat study, spirotetramat did not provide any qualitative or quantitative evidence of a neurotoxic potential. In addition to the specific neurotoxicity testing, no treatment-related clinical signs, changes in absolute brain weight, neuropathological, or neurobehavioral findings were noted in the general toxicity studies (i.e. acute, subacute, subchronic, developmental, reproduction, and chronic). Of the products being compared to spirotetramat in this section, three of the actives, unlike spirotetramat, have cholinesterase inhibiting properties (dimethoate, malathion, and oxydemeton-methyl) and four actives showed evidence of inducing neurological toxicity (dimethoate, imidacloprid, oxydemeton-methyl, and thiamethoxam).

In vivo and *in vitro* mutagenicity studies with spirotetramat and its metabolites indicate that spirotetramat is not mutagenic. Of the products being compared to spirotetramat in this section, three actives (dimethoate, imidacloprid, and oxydemeton-methyl) showed some evidence of positive responses (*in vivo* and/or *in vitro*) in gene mutational testing or cytogenetic testing.

The chronic population adjusted dose (cPAD) for spirotetramat is based on the repeated dose 1-year oral toxicity study in the dog, which established a NOAEL of 6 mg/kg bw/day (males). Applying a 100-fold uncertainty factor, the cPAD is 0.06 mg/kg bw/day. Of the products that are being compared to spirotetramat in this section, many of the cPADs are orders of magnitude lower than spirotetramat.

These findings suggest an overall favorable toxicology package for spirotetramat compared to the alternative products used in minor-use Brassica (cole) leafy vegetable crops.

Alternatives Pose Greater Risk to the Environment

Risk assessments demonstrate that spirotetramat 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 13 is a comparison based on Tier 1 risk quotients taken from the reduced risk submissions in which quantitative values of these risk quotients are provided.

Table 13. Summary of Ecological Risk for Spirotetramat and Major Alternative Products for Use on Brassica (Cole) Leafy Vegetables: Broccoli, Broccoli raab (rapini), Brussels sprouts, Cabbage, Cauliflower, Cavalo broccolo, Chinese broccoli (gai lon), Chinese cabbage (bok choy), Chinese cabbage (napa), Chinese mustard cabbage (gai choy), Collards, Kale, Kohlrabi, Mizuna, Mustard greens, Mustard spinach, and Rape Greens.

Chemical	Avian Acute	Avian Chronic	Mammal Acute	Mammal Chronic	Fish Acute	Fish Chronic	Daphnia Acute	Daphnia Chronic	Marine Acute	Bees[1]
Spirotetramat	**0.01**	**2.43**	**0.02**	**0.45**	**<0.01**	**<0.01**	**<0.01**	**<0.01**	**<0.01**	**>100**
(Beta)-Cyfluthrin	0.08	0.42	2.84	2.12	5.96	39.7	1.4	57.3	202.5	0.012
Dimethoate	0.12	30.00	0.29	69.41	<0.01	<0.01	<0.01	0.05	<0.01	0.16
Imidacloprid	0.07	2.32	0.11	2.63	<0.01	<0.01	<0.01	<0.01	0.17	0.04
Lambda- Cyhalothrin	0.42	179.57	6.96	29.93	64.0	208.0	55.56	135000	1020.0	0.038
Malathion	0.09	>0.86	0.13	130.14	0.02	0.01	0.70	3.83	0.32	0.709
Oxydemeton-methyl	1.93	233.22	3.79	404.69	0.01	<0.01	0.03	0.13	<0.01	0.54
Thiamethoxam	<0.01	<0.10	0.01	21.69	<0.01	<0.01	<0.01	<0.01	<0.01	0.024

No Tier 1 LOC exceedances, or for honey bees, practically non-toxic

Between the endangered species LOC and the high risk LOC for acute risk. Between 1 and 5 times the LOC for chronic risk or for honey bees, moderately toxic.

Greater than the high risk LOC for acute risk. Greater than 5X the LOC for chronic risk. Highly toxic to honey bees.

[1]The "Bees" column gives the 48 h contact LD50 value since there is no EPA risk paradigm for bees with the color indicative of the hazard classification as noted above.

On an acre for acre replacement, the use of spirotetramat reduces the amount of active ingredient applied when compared to most alternative products. Dimethoate and imidacloprid are applied at similar rates; all other alternative insecticide groups, especially the organophosphate insecticides have much higher seasonal application rates than spirotetramat.

In addition to low application rates, spirotetramat can reduce the environmental burden associated with retreatment of resurgent pest populations. This is possible because of two other unique properties of spirotetramat: (1) systemic movement allows control of pest infestations hidden in dense crop canopies and (2) reduced fecundity of adult female insects extends residual control into the next pest generation.

The estimated ground water concentration for spirotetramat is negligible (i.e., consumes zero percent of the cPAD). This is true even after considering the combined residues of spirotetramat and its degradates. Spirotetramat degrades rapidly in soil and water, leading to low estimated concentrations in aquatic environments. Human exposure to spirotetramat residues in water is anticipated to be negligible consuming 0% of the cPAD for all population subgroups. By comparison, estimated drinking water concentrations consume most or all of the cPAD for many of the alternatives. Therefore, among the alternative compounds, only spirotetramat is expected to have low surface water as well as low ground water contamination risks.

Spirotetramat has minimal acute, adult risk to bees (LD_{50} >100 µg a.i./bee; practically non-toxic). For Brassica(cole) leafy vegetables, spirotetramat compares very favorably to alternative products and is the least toxic insecticide to honeybees, characterized as "practically non-toxic" to honey bees. All of the alternative insecticides are characterized as "highly toxic" to bees (contact LD_{50} <1 µg/bee).

Bayer CropScience has conducted a comprehensive honey bee safety research and evaluation program. Field studies designed to evaluate safety to bees following a field exposure to spirotetramat at bloom have been conducted in *Phacelia*, melon and citrus. There were no adverse effects to bees or colony health noted in these studies.

These findings suggest an overall favorable environmental package for spirotetramat compared to the alternative products used in minor-use Brassica (cole) vegetable crops.

4.3.2 – FIFRA Criterion III: The minor use pesticide plays or will play a significant part in managing pest resistance

Green peach aphid, potato aphid, turnip aphid, and cabbage aphid are commonly found in broccoli (46,47), cabbage (48,49,50), cauliflower (51,52), broccoli raab (rapini) (53,54), Brussels sprouts (55,56), collards (57, 58), bok choy (59,60), napa (61), kohlrabi (62), kale (58,63), and other members of the Brassica (Cole) Leafy Vegetables crop grouping (58, 59) . One of the more common aphids within this group is the green peach aphid and on a global level, including the U.S., there have been 392 documented cases of resistance in green peach aphid to members of the organophosphate, carbamate, pyrethroid, neonicotinoid, and other chemical classes (64); as seen in Table 10, the alternatives to spirotetramat are from the organophosphate (3 active ingredients), pyrethroid (2 active ingredients), and neonicotinoid (2 active ingredients) chemical classes and thus, additional modes of action are needed for implementation into resistance management strategies for control of this pest. In biological evaluations by university researchers, spirotetramat, a new mode of action against aphids, has shown excellent control of green peach aphids, among others (65,66) and will help preserve the existing modes of action in this market.

4.3.3 - FIFRA Criterion IV: The minor use pesticide plays or will play a significant part in an integrated pest management program

Beneficial parasitoids and predators serve to maintain aphid populations below the economic threshold; however, they are usually unable to completely control aphid populations. Lady beetle larvae, lacewing larvae, syrphid fly larvae and aphid parasites are some of the beneficial insects used to control aphids (46,52, 69). The low impact on beneficial arthropods, coupled with the high level of efficacy, has led to spirotetramat being listed in university recommendations in various cole crops (67,68,70).

4.4 - Leafy Vegetables: Amaranth, Arugula, Cardoon, Celery, Celtuce, Chervil, Chinese Celery, Chrysanthemum, Corn Salad, Cress, Dandelion, Dock, Endive (Escarole), Florence Fennel, Head and Leaf Lettuce, Orach, Parsley, Purslane, Radicchio, Rhubarb, Spinach, and Swiss Chard

Like other minor-use crops, many of the members of the leafy vegetable crop grouping are extremely minor in acreage, to the point where no specific recommendations or other information exists for which to cite in this section. However, the key pests infesting all members of the leafy vegetable crop grouping are various species of aphids. Table 14 provides a summary of the major alternative insecticides presently registered for control of aphids in these minor-use crops. Each of the alternative products listed in Table 14, arranged in order of percent market share from high to low, account for more than 5% of the foliar treated acres.

Table 14. Alternatives to Spirotetramat for Use on Leafy Vegetables: Amaranth, Arugula, Cardoon, Celery, Celtuce, Chervil, Chinese Celery, Chrysanthemum, Corn Salad, Cress, Dandelion, Dock, Endive (Escarole), Florence Fennel, Head and Leaf Lettuce, Orach, Parsley, Purslane, Radicchio, Rhubarb, Spinach, and Swiss Chard.

Active Ingredient	Brand	IRAC Group	Mode of Action
SPIROTETRAMAT	**MOVENTO**	**23**	**Inhibitor of Acetyl CoA carboxylase**
IMIDACLOPRID	ADMIRE PRO	4A	Nicotinic acetylcholine receptor agonist
PERMETHRIN	PERM-UP	3	Sodium channel modulator
LAMBDA-CYHALOTHRIN	WARRIOR	3	Sodium channel modulator
ACETAMIPRID	ASSAIL	4A	Nicotinic acetylcholine receptor agonist
FLONICAMID	BELEAF	9C	Selective homopteran feeding blockers
METHOMYL	LANNATE	1A	Acetylcholinesterase inhibitor
MALATHION	MALATHION	1B	Acetylcholinesterase inhibitor

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

Alternatives Pose Greater Risk to Human Health

Acute toxicity evaluations of the spirotetramat end-use product MOVENTO® and alternative end-use insecticides are summarized in Table 15 with additional comments below.

Table 15. Comparison of the Toxicity Categories and Signal Words of Spirotetramat End-Use Products with Alternative End-Use Insecticides for Use on Leafy Vegetables: Amaranth, Arugula, Cardoon, Celery, Celtuce, Chervil, Chinese Celery, Chrysanthemum, Corn Salad, Cress, Dandelion, Dock, Endive (Escarole), Florence Fennel, Head and Leaf Lettuce, Orach, Parsley, Purslane, Radicchio, Rhubarb, Spinach, and Swiss Chard.

Active Ingredient	Trade Name	Toxicity Category	Signal Word
Spirotetramat	**MOVENTO®**	III	Caution
Acetamiprid	Assail® 70WP	III	Caution
Flonicamid	Beleaf®	III	Caution
Imidacloprid	Admire® Pro	III	Caution
Lambda-Cyhalothrin	Warrior®	II	Warning
Malathion	Malathion 5 EC	II	Warning
Methomyl	Lannate®	I	Danger
Permethrin	Perm-Up®	II	Warning

The spirotetramat end-use product MOVENTO® carries the signal word "Caution" (Category III) based on oral, dermal, and eye irritation hazards. This formulation demonstrates low toxicity by the oral, dermal, and inhalation routes of exposure. Of the seven end-use products being compared to spirotetramat in this section, one product has a Category I (Danger) classification, three products have a Category II (Warning) classification, and three products have a Category III (Caution) classification. Therefore, four of the seven alternative products carry more hazardous acute toxicity classifications than the spirotetramat end-use product MOVENTO®.

Toxicity evaluations of spirotetramat and alternative insecticides are summarized in Table 16 with additional comments below.

Table 16. Active Ingredient Toxicology Summary for Spirotetramat and Major Alternative Insecticides for Use on Leafy Vegetables: Amaranth, Arugula, Cardoon, Celery, Celtuce,

Chervil, Chinese Celery, Chrysanthemum, Corn Salad, Cress, Dandelion, Dock, Endive (Escarole), Florence Fennel, Head and Leaf Lettuce, Orach, Parsley, Purslane, Radicchio, Rhubarb, Spinach, and Swiss Chard.

Chemical (Technical)	Acute Toxicity	Geno-toxicity	Repro-ductive Toxicity (Primary Evidence)	Develop-mental Toxicity (Primary Evidence)	Onco-genicity Class [d]	Q_1^* (mg/kg/day)$^{-1}$	Chronic Ref Dose (mg/kg/day)
Spirotetramat	**Warning**	–[a]	–	–	E	–	**0.132**
Acetamiprid	Warning	+/- [b]	–	–	E	–	0.023
Flonicamid	Caution	–	–	–	S	–	0.04
Imidacloprid	Warning	+/-	–	–	E	–	0.057
Lambda-Cyhalothrin	Warning	–	–	–	E	–	0.001
Malathion	Warning	+[c]	–	–	S		0.07
Methomyl	Danger	–	–	–	E	–	0.008
Permethrin	Caution	–	–	–	Likely	9.6×10^{-3}	0.25

[a] "-" indicates no evidence within a particular category
[b] "+/-" indicates positive and negative findings were observed
[c] "+" indicates positive findings within a category
[d] E: not likely; C: possible; S: suggestive; B2: probable
[e] Weak evidence for genotoxicity

Spirotetramat, registered by EPA on October 15, 2010, is a new, safer chemistry that will replace organophosphates, neonicotinoids, pyrethroids and other chemistries because of its unique systemicity and broad pest spectrum. Spirotetramat showed no evidence of oncogenicity in any of the studies conducted in the rat and mouse and is therefore, classified as *not likely to be carcinogenic to humans (Class E)*. One of the alternative products (permethrin) is classified as a *likely human carcinogen* and two (flonicamid and malathion) as *suggestive evidence of carcinogenic potential* (Class S). The remaining products are classified as *not likely to be carcinogenic in humans* (Class E).

The reproductive and prenatal developmental toxicity studies in rats and rabbits provided no evidence to suggest that spirotetramat possesses either a teratogenic or primary toxicological potential, as non-maternal toxicity was identified at equivalent or higher doses than maternal toxicity in both species. The parental, reproductive, and offspring NOAELs (mg/kg/day) of many of the comparative products are, in general, significantly lower than the male (M) / female (F) parental, reproductive, and offspring NOAELs determined for spirotetramat.

Based on specific neurotoxicity screening assessments conducted acutely in the rat and incorporated as a satellite investigation as part of the 1-year chronic rat study, spirotetramat did not provide any qualitative or quantitative evidence of a neurotoxic potential. In addition to the specific neurotoxicity testing, no treatment-related clinical signs, changes in absolute brain weight, neuropathological, or neurobehavioral findings were noted in the general toxicity studies (i.e. acute, subacute, subchronic, developmental, reproduction, and chronic). Of the products being compared to spirotetramat in this section, two of the actives, unlike spirotetramat, have cholinesterase inhibiting properties (malathion and methomyl) and two actives showed evidence of inducing neurological toxicity (acetamiprid and imidacloprid).

In vivo and *in vitro* mutagenicity studies with spirotetramat and its metabolites indicate that spirotetramat is not mutagenic. Of the products being compared to spirotetramat in this section, three

actives (acetamiprid, imidacloprid, and malathion) showed some evidence of positive responses (*in vivo* and/or *in vitro*) in gene mutational testing or cytogenetic testing.

The chronic population adjusted dose (cPAD) for spirotetramat is based on the repeated dose 1-year oral toxicity study in the dog, which established a NOAEL of 6 mg/kg bw/day (males). Applying a 100-fold uncertainty factor, the cPAD is 0.06 mg/kg bw/day. Of the products that are being compared to spirotetramat in this section, many of the cPADs are orders of magnitude lower than spirotetramat.

These findings suggest an overall favorable toxicology package for spirotetramat compared to the alternative products used in minor-use leafy vegetable crops.

Alternatives Pose Greater Risk to the Environment

Risk assessments demonstrate that spirotetramat 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 17 is a comparison based on Tier 1 risk quotients taken from the reduced risk submissions in which quantitative values of these risk quotients are provided.

Table 17. Summary of Ecological Risk for Spirotetramat and Major Alternative Products for Use on Leafy Vegetables: Amaranth, Arugula, Cardoon, Celery, Celtuce, Chervil, Chinese Celery, Chrysanthemum, Corn Salad, Cress, Dandelion, Dock, Endive (Escarole), Florence Fennel, Head and Leaf Lettuce, Orach, Parsley, Purslane, Radicchio, Rhubarb, Spinach, and Swiss Chard.

Chemical	Avian Acute	Avian Chronic	Mammal Acute	Mammal Chronic	Fish Acute	Fish Chronic	Daphnia Acute	Daphnia Chronic	Marine Acute	Bees[1]
Spirotetramat	**0.01**	**2.43**	**0.02**	**0.45**	**<0.01**	**<0.01**	**<0.01**	**<0.01**	**<0.01**	**>100**
Acetamiprid	<0.02	0.47	0.24	7.9	<0.01	<0.01	<0.01	<0.01	0.09	8.09
Flonicamid										
Imidacloprid	0.07	2.32	0.11	2.63	<0.01	<0.01	<0.01	<0.01	0.17	0.04
Lambda- Cyhalothrin	0.42	179.57	6.96	29.93	64.0	208.0	55.56	135000	1020.0	0.038
Malathion	0.09	>0.86	0.13	130.14	0.02	0.01	0.70	3.83	0.32	0.709
Methomyl	0.39	4.76	21.20	9.52	0.26	1.95	14.77	205	5.21	<0.5
Permethrin	0.03	0.59	0.04	2.57	6.73	3.4	136.4	33.9	280.0	0.13

No Tier 1 LOC exceedances, or for honey bees, practically non-toxic

Between the endangered species LOC and the high risk LOC for acute risk. Between 1 and 5 times the LOC for chronic risk or for honey bees, moderately toxic.

Greater than the high risk LOC for acute risk. Greater than 5X the LOC for chronic risk. Highly toxic to honey bees.

No data available for comparison.

[1]The "Bees" column gives the 48 h contact LD50 value since there is no EPA risk paradigm for bees with the color indicative of the hazard classification as noted above.

On an acre for acre replacement, the use of spirotetramat reduces the amount of active ingredient applied when compared to most alternative products. Acetamiprid and imidacloprid are applied at similar rates. Most notable among the alternative insecticide groups, the organophosphate and carbamate insecticides have much higher seasonal application rates than spirotetramat.

In addition to low application rates, spirotetramat can reduce the environmental burden associated with retreatment of resurgent pest populations. This is possible because of two other unique properties of spirotetramat: (1) systemic movement allows control of pest infestations hidden in dense crop canopies and (2) reduced fecundity of adult female insects extends residual control into the next pest generation.

The estimated ground water concentration for spirotetramat is negligible (i.e., consumes zero percent of the cPAD). This is true even after considering the combined residues of spirotetramat and its degradates. Spirotetramat degrades rapidly in soil and water, leading to low estimated concentrations in aquatic environments. Human exposure to spirotetramat residues in water is anticipated to be negligible consuming 0% of the cPAD for all population subgroups. By comparison, estimated drinking water concentrations consume most or all of the cPAD for many of the alternatives. Therefore, among the alternative compounds, only spirotetramat is expected to have low surface water as well as low ground water contamination risks.

Spirotetramat has minimal acute, adult risk to bees (LD_{50} >100 µg a.i./bee; practically non-toxic). For leafy vegetables, spirotetramat compares very favorably to alternative products and is the least toxic insecticide to honeybees, characterized as "practically non-toxic" to honey bees. All of the alternative insecticides, with the exception of acetamiprid, are characterized as "highly toxic" to bees (contact LD_{50} <1 µg/bee).

Bayer CropScience has conducted a comprehensive honey bee safety research and evaluation program. Field studies designed to evaluate safety to bees following a field exposure to spirotetramat at bloom have been conducted in *Phacelia*, melon and citrus. There were no adverse effects to bees or colony health noted in these studies.

These findings suggest an overall favorable environmental package for spirotetramat compared to the alternative products used in minor-use leafy vegetable crops

4.4.2 – FIFRA Criterion III: The minor use pesticide plays or will play a significant part in managing pest resistance

Green peach aphid, lettuce aphid, black bean aphid, foxglove aphid, and other aphid species commonly or occasionally infest arugula (59,71,72), celery (73,74,75,76), chrysanthemum (77), dandelion (78), endive/escarole (79), Florence fennel (80,81), head and leaf lettuce (82,83,84,85,86,87), and other members of the leafy vegetable crop grouping (88,89,90,91,92,93,94) . One of the more common aphids found on the minor-use leafy vegetables is the green peach aphid, which can also vector diseases of leafy vegetables (75,83) and on a global level, including the U.S., there have been 392 documented cases of resistance development in green peach aphid to members of the organophosphate, carbamate, pyrethroid, neonicotinoids, and other chemical classes(64); this is likely due to the pest's very wide host range and levels of exposure. In lettuce aphid, there have been 10 documented cases of resistance development to organophosphates, pyrethroids, and other chemical classes and in black bean aphid, 4 cases, largely to members of the organophosphate chemical class. As seen in Table 14, the major alternatives to spirotetramat are from the carbamate (1 active ingredient), organophosphate (1 active ingredient), pyrethroid (2 active ingredients), neonicotinoid (2 active ingredients), and pyridinecarboxamide (1 active ingredient) chemical classes; having this limited number of modes of action/chemical classes available in these minor-use crops places extreme selection pressure on these resistance-prone aphid species to the available chemistries. The regulatory approval of spirotetramat for use on these minor-use crops not only provided growers with a highly efficacious tool for management of aphids but also delivered a new mode of action for resistance management. In biological evaluations by university researchers, spirotetramat has shown excellent

control of green peach and lettuce aphids, among others (95,96,97,98,99) and will help preserve the existing modes of action in this market.

4.4.3 - FIFRA Criterion IV: The minor use pesticide plays or will play a significant part in an integrated pest management program

Beneficial parasitoids and predators can serve to maintain aphid populations below the economic threshold under low population densities; however, due to the high reproductive rate of aphids, they are usually unable to completely control aphid populations and can actually serve as produce contaminants themselves, particularly at time periods approaching harvest (91). Lady beetle larvae, lacewing larvae, syrphid fly larvae, minute pirate bugs, and aphid parasites are some of the insects used to control aphids (73,82,83,84,92). Growers are aware of the importance of beneficial insects and try to utilize products that are least damaging to natural populations of beneficials (75). The low impact on beneficial arthropods, coupled with the high level of efficacy, has led to spirotetramat being listed in university recommendations in various minor-use leafy vegetable crops (100,101,102,103,104,105).

4.5 - Globe Artichoke

Key pests infesting globe artichoke for which spirotetramat has been labeled are various species of aphids, namely artichoke aphid, black bean aphid, and green peach aphid (106,107). Table 18 provides a summary of the major alternative insecticides presently registered for control of aphids in artichoke. Each of the alternative products listed in Table 18, arranged in order of percent market share from high to low, account for more than 5% of the foliar treated acres.

Table 18. Alternatives to Spirotetramat for Use on Globe Artichoke for Aphid Control

Active Ingredient	Brand	IRAC Group	Mode of Action
SPIROTETRAMAT	**MOVENTO**	**23**	**Inhibitor of Acetyl CoA carboxylase**
THIAMETHOXAM	ACTARA	4A	Nicotinic acetylcholine receptor agonist
IMIDACLOPRID	ADMIRE PRO	4A	Nicotinic acetylcholine receptor agonist
PYRETHRINS	PYGANIC	3A	Sodium channel modulator
AZADIRACHTIN	AZA-DIRECT	UN	Compounds of unknown or uncertain MoA

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

Alternatives Pose Greater Risk to Human Health

Acute toxicity evaluations of the spirotetramat end-use product MOVENTO® and alternative end-use insecticides are summarized in Table 19 with additional comments below.

Table 19. Comparison of the Toxicity Categories and Signal Words of Spirotetramat End-Use Product with Alternative End-Use Insecticides for Use on Globe Artichoke.

Active Ingredient	Trade Name	Toxicity Category	Signal Word
Spirotetramat	**MOVENTO®**	III	Caution
Azadirachtin	Aza-Direct®	III	Caution
Imidacloprid	Admire® Pro	III	Caution

Active Ingredient	Trade Name	Toxicity Category	Signal Word
Pyrethrins	Pyganic®	III	Caution
Thiamethoxam	Platinum®	III	Caution

The spirotetramat end-use product MOVENTO® carries the signal word "Caution" (Category III) based on oral, dermal, and eye irritation hazards. This formulation demonstrates low toxicity by the oral, dermal, and inhalation routes of exposure. Of the four end-use products being compared to spirotetramat in this section, all have a Category III (Caution) classification.

Toxicity evaluations of spirotetramat and alternative insecticides are summarized in Table 20 with additional comments below.

Table 20. Active Ingredient Toxicology Summary for Spirotetramat and Major Alternative Insecticides for Use on Globe Artichoke.

Chemical (Technical)	Acute Toxicity	Geno-toxicity	Repro-ductive Toxicity (Primary Evidence)	Develop-mental Toxicity (Primary Evidence)	Onco-genicity Class [d]	Q_1* (mg/kg/day)$^{-1}$	Chronic Ref Dose (mg/kg/day)
Spirotetramat	**Warning**	–[a]	–	–	E	–	**0.132**
Azadirachtin	Caution	-	-	-	NA	NA	NA
Imidacloprid	Warning	+/- [b]	–	–	E	–	0.057
Pyrethrins	Caution	–	+ [c]	–	S	–	0.044
Thiamethoxam	Caution	–	–	–	C	3.77	0.0006

[a] "–" indicates no evidence within a particular category
[b] "+/-" indicates positive and negative findings were observed
[c] "+" indicates positive findings within a category
[d] E: not likely; C: possible; S: suggestive; B2: probable

Spirotetramat, registered by EPA on October 15, 2010, is a new, safer chemistry that will replace organophosphates, neonicotinoids, pyrethroids and other chemistries because of its unique systemicity and broad pest spectrum. Spirotetramat showed no evidence of oncogenicity in any of the studies conducted in the rat and mouse and is therefore, classified as *not likely to be carcinogenic to humans (Class E).* One of the alternative products (thiamethoxam) is classified as a *possible human carcinogen* (Class C) and one (pyrethrins) as *suggestive evidence of carcinogenic potential* (Class S). Imidacloprid is classified as *not likely to be carcinogenic in humans* (Class E) and no information readily exists for azadirachtin.

The reproductive and prenatal developmental toxicity studies in rats and rabbits provided no evidence to suggest that spirotetramat possesses either a teratogenic or primary toxicological potential, as non-maternal toxicity was identified at equivalent or higher doses than maternal toxicity in both species. Pyrethrins have shown positive evidence of reproductive toxicity. The parental, reproductive, and offspring NOAELs (mg/kg/day) of the remaining comparative products are, in general, significantly lower than the male (M) / female (F) parental, reproductive, and offspring NOAELs determined for spirotetramat.

Based on specific neurotoxicity screening assessments conducted acutely in the rat and incorporated as a satellite investigation as part of the 1-year chronic rat study, spirotetramat did not provide any

qualitative or quantitative evidence of a neurotoxic potential. In addition to the specific neurotoxicity testing, no treatment-related clinical signs, changes in absolute brain weight, neuropathological, or neurobehavioral findings were noted in the general toxicity studies (i.e. acute, subacute, subchronic, developmental, reproduction, and chronic). Of the products being compared to spirotetramat in this section, two actives showed evidence of inducing neurological toxicity (imidacloprid and thiamethoxam).

In vivo and *in vitro* mutagenicity studies with spirotetramat and its metabolites indicate that spirotetramat is not mutagenic. Of the products being compared to spirotetramat in this section, one active (imidacloprid) showed some evidence of positive responses (*in vivo* and/or *in vitro*) in gene mutational testing or cytogenetic testing.

The chronic population adjusted dose (cPAD) for spirotetramat is based on the repeated dose 1-year oral toxicity study in the dog, which established a NOAEL of 6 mg/kg bw/day (males). Applying a 100-fold uncertainty factor, the cPAD is 0.06 mg/kg bw/day. Of the products that are being compared to spirotetramat in this section, many of the cPADs are orders of magnitude lower than spirotetramat.

These findings suggest an overall favorable toxicology package for spirotetramat compared to the alternative products used in globe artichoke crops.

Alternatives Pose Greater Risk to the Environment

Risk assessments demonstrate that spirotetramat 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 21 is a comparison based on Tier 1 risk quotients taken from the reduced risk submissions in which quantitative values of these risk quotients are provided.

Table 21. Summary of Ecological Risk for Spirotetramat and Major Alternative Products for Use on Globe Artichoke.

Chemical	Avian Acute	Avian Chronic	Mammal Acute	Mammal Chronic	Fish Acute	Fish Chronic	Daphnia Acute	Daphnia Chronic	Marine Acute	Bees[1]
Spirotetramat	**0.01**	**2.43**	**0.02**	**0.45**	**<0.01**	**<0.01**	**<0.01**	**<0.01**	**<0.01**	**>100**
Azadirachtin	0.02	0.09	0.01	0.33	0.03	0.17	<0.01	<0.01	NA[2]	>11.8
Imidacloprid	0.07	2.32	0.11	2.63	<0.01	<0.01	<0.01	<0.01	0.17	0.04
Pyrethrins	0.02	0.78	0.06	0.97	0.54	0.19	0.24	0.70	1.98	0.022
Thiamethoxam	<0.01	<0.10	0.01	21.69	<0.01	<0.01	<0.01	<0.01	<0.01	0.024

No Tier 1 LOC exceedances, or for honey bees, practically non-toxic

Between the endangered species LOC and the high risk LOC for acute risk. Between 1 and 5 times the LOC for chronic risk or for honey bees, moderately toxic.

Greater than the high risk LOC for acute risk. Greater than 5X the LOC for chronic risk. Highly toxic to honey bees.

[1]The "Bees" column gives the 48 h contact LD50 value since there is no EPA risk paradigm for bees with the color indicative of the hazard classification as noted above.

[2] NA = Not available

On an acre for acre replacement, the use of spirotetramat is similar in the amount of active ingredient applied compared to the alternative products. However, spirotetramat can reduce the environmental burden associated with retreatment of resurgent pest populations. This is possible because of two other unique properties of spirotetramat: (1) systemic movement allows control of pest infestations

hidden in dense crop canopies and (2) reduced fecundity of adult female insects extends residual control into the next pest generation.

The estimated ground water concentration for spirotetramat is negligible (i.e., consumes zero percent of the cPAD). This is true even after considering the combined residues of spirotetramat and its degradates. Spirotetramat degrades rapidly in soil and water, leading to low estimated concentrations in aquatic environments. Human exposure to spirotetramat residues in water is anticipated to be negligible consuming 0% of the cPAD for all population subgroups. Spirotetramat is expected to have low surface water as well as low ground water contamination risks.

Spirotetramat has minimal acute, adult risk to bees (LD_{50} >100 µg a.i./bee; practically non-toxic). For globe artichoke, spirotetramat compares very favorably to alternative products and is the least toxic insecticide to honeybees, characterized as "practically non-toxic" to honey bees. All of the alternative insecticides, with the exception of azadirachtin, are characterized as "highly toxic" to bees (contact LD_{50} <1 µg/bee).

Bayer CropScience has conducted a comprehensive honey bee safety research and evaluation program. Field studies designed to evaluate safety to bees following a field exposure to spirotetramat at bloom have been conducted in *Phacelia*, melon and citrus. There were no adverse effects to bees or colony health noted in these studies.

These findings suggest an overall favorable environmental package for spirotetramat compared to the alternative products used in globe artichoke.

4.5.2 – FIFRA Criterion III: The minor use pesticide plays or will play a significant part in managing pest resistance

As stated previously in other sections of this document, there have been 392 documented cases of resistance development in green peach aphid to members of the organophosphate, carbamate, pyrethroid, neonicotinoids, and other chemical classes. In black bean aphid, 4 cases, largely to members of the organophosphate chemical class and to date, no documented cases have been reported in artichoke aphid (64) . As seen in Table 18 above, aside from spirotetramat, only four active ingredients are registered for control of aphids on artichoke: two of these are from the neonicotinoid chemical class, IRAC Group 4A, to which green peach aphid has developed resistance in certain crops; one is from IRAC Group 3A to which green peach aphid has also developed resistance in certain crops; the last is a biologically-derived product with an unknown mode of action. In short, additional modes of action were needed in this market for rotational purposes to maintain all of the existing product's effectiveness for control of aphids and this, along with the excellent residual efficacy against aphids in artichoke (108), likely served as the basis for a Pesticide Clearance Request being submitted to IR-4 for spirotetramat.

4.5.3 - FIFRA Criterion IV: The minor use pesticide plays or will play a significant part in an integrated pest management program

Native predacious beetles may mitigate aphid infestations but have been ineffective at maintaining population densities below the economic threshold (106). Several parasitic wasps attack aphids in artichoke, as well as general predators including lady beetles, syrphid fly, and lacewings also consume aphids. However, naturally occurring predators and parasites rarely provide timely control because of considerable time lag between the build-up of the parasite/predator populations and the aphid populations (109). The use of broad-spectrum insecticides for control of artichoke plume moth, such as pyrethroids, have a significant negative impact on beneficial parasites and predators of various

aphid species and it is doubtful if augmentation of beneficial populations would be successful due to this fact (106). On artichokes grown in isolated small areas in the southern deserts where insecticide use is minimum (0-3 applications per year), growers have released convergent lady beetles for aphid control with some success (110). As indicated in the introductory sections of this document, lab and field studies have shown spirotetramat to have low impact on beneficial predators and parasites, including those found in artichoke production systems, which will allow an integrated pest management system to flourish.

4.6 - Pomegranate

Key pests infesting pomegranate for which spirotetramat has been labeled are aphids, predominantly cotton aphid, and greenhouse whitefly (111,112). Table 22 provides a summary of the major alternative insecticides presently registered for control of aphids and whitefly in pomegranate. With the exception of spirotetramat, only one alternative product exists, clearly showing the need for additional products in this minor-use segment.

Table 22. Alternative to Spirotetramat for Use on Pomegranate for Aphid and Whitefly Control.

Active Ingredient	Brand	IRAC Group	Mode of Action
SPIROTETRAMAT	MOVENTO	23	Inhibitor of Acetyl CoA carboxylase
IMIDACLOPRID	ADMIRE PRO	4A	Nicotinic acetylcholine receptor agonist

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

Alternatives Pose Greater Risk to Human Health

Acute toxicity evaluations of the spirotetramat end-use product MOVENTO® and the alternative end-use insecticide is summarized in Table 23 with additional comments below.

Table 23. Comparison of the Toxicity Categories and Signal Words of Spirotetramat End-Use Products with the Alternative End-Use Insecticide for Use on Pomegranate.

Active Ingredient	Trade Name	Toxicity Category	Signal Word
Spirotetramat	**MOVENTO®**	III	Caution
Imidacloprid	Admire® Pro	III	Caution

The spirotetramat end-use product MOVENTO® carries the signal word "Caution" (Category III) based on oral, dermal, and eye irritation hazards. This formulation demonstrates low toxicity by the oral, dermal, and inhalation routes of exposure. The alternative product also carries the signal word "Caution" classification.

Toxicity evaluations of spirotetramat and the alternative insecticide are summarized in Table 24 with additional comments below.

Table 24. Active Ingredient Toxicology Summary for Spirotetramat and the Alternative Insecticide for Use on Pomegranate.

Chemical (Technical)	Acute Toxicity	Geno-toxicity	Repro-ductive Toxicity (Primary Evidence)	Develop-mental Toxicity (Primary Evidence)	Onco-genicity Class [c]	Q_1^* (mg/kg/day)$^{-1}$	Chronic Ref Dose (mg/kg/day)
Spirotetramat	**Warning**	**–[a]**	–	–	**E**	–	**0.132**
Imidacloprid	Warning	+/- [b]	–	–	E	–	0.057

[a] "-" indicates no evidence within a particular category
[b] "+/-" indicates positive and negative findings were observed
[c] E: not likely; C: possible; S: suggestive; B2: probable

Spirotetramat, registered by EPA on October 15, 2010, is a new, safer chemistry that will replace organophosphates, neonicotinoids, pyrethroids and other chemistries because of its unique systemicity and broad pest spectrum. Spirotetramat showed no evidence of oncogenicity in any of the studies conducted in the rat and mouse and is therefore, classified as *not likely to be carcinogenic to humans (Class E).* Imidacloprid is also classified as *not likely to be carcinogenic in humans* (Class E).

The reproductive and prenatal developmental toxicity studies in rats and rabbits provided no evidence to suggest that spirotetramat possesses either a teratogenic or primary toxicological potential, as non-maternal toxicity was identified at equivalent or higher doses than maternal toxicity in both species.

Based on specific neurotoxicity screening assessments conducted acutely in the rat and incorporated as a satellite investigation as part of the 1-year chronic rat study, spirotetramat did not provide any qualitative or quantitative evidence of a neurotoxic potential. In addition to the specific neurotoxicity testing, no treatment-related clinical signs, changes in absolute brain weight, neuropathological, or neurobehavioral findings were noted in the general toxicity studies (i.e. acute, subacute, subchronic, developmental, reproduction, and chronic). Imidacloprid showed evidence of inducing neurological toxicity.

In vivo and *in vitro* mutagenicity studies with spirotetramat and its metabolites indicate that spirotetramat is not mutagenic. Imidacloprid showed some evidence of positive responses (*in vivo* and/or *in vitro*) in gene mutational testing or cytogenetic testing.

The comparison to imidacloprid suggests an overall more favorable toxicology package for spirotetramat.

Alternatives Pose Greater Risk to the Environment

Risk assessments demonstrate that spirotetramat 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 25 is a comparison based on Tier 1 risk quotients taken from the reduced risk submissions in which quantitative values of these risk quotients are provided.

Table 25. Summary of Ecological Risk for Spirotetramat and the Alternative Product for Use on Pomegranate.

Chemical	Avian Acute	Avian Chronic	Mammal Acute	Mammal Chronic	Fish Acute	Fish Chronic	Daphnia Acute	Daphnia Chronic	Marine Acute	Bees[1]
Spirotetramat	0.01	2.43	0.02	0.45	<0.01	<0.01	<0.01	<0.01	<0.01	>100
Imidacloprid	0.07	2.32	0.11	2.63	<0.01	<0.01	<0.01	<0.01	0.17	0.04

No Tier 1 LOC exceedances, or for honey bees, practically non-toxic

Between the endangered species LOC and the high risk LOC for acute risk. Between 1 and 5 times the LOC for chronic risk or for honey bees, moderately toxic.

Greater than the high risk LOC for acute risk. Greater than 5X the LOC for chronic risk. Highly toxic to honey bees.

[1]The "Bees" column gives the 48 h contact LD50 value since there is no EPA risk paradigm for bees with the color indicative of the hazard classification as noted above.

On an acre for acre replacement, the use of spirotetramat reduces the amount of active ingredient applied when compared to imidacloprid on a seasonal basis. This is possible because of two other unique properties of spirotetramat: (1) systemic movement allows control of pest infestations hidden in dense crop canopies and (2) reduced fecundity of adult female insects extends residual control into the next pest generation.

The estimated ground water concentration for spirotetramat is negligible (i.e., consumes zero percent of the cPAD). This is true even after considering the combined residues of spirotetramat and its degradates. Spirotetramat degrades rapidly in soil and water, leading to low estimated concentrations in aquatic environments. Human exposure to spirotetramat residues in water is anticipated to be negligible consuming 0% of the cPAD for all population subgroups. Spirotetramat is expected to have low surface water as well as low ground water contamination risks.

Spirotetramat has minimal acute, adult risk to bees (LD_{50} >100 µg a.i./bee; practically non-toxic). Conversely, imidacloprid is characterized as "highly toxic" to bees (contact LD_{50} <1 µg/bee).

Bayer CropScience has conducted a comprehensive honey bee safety research and evaluation program. Field studies designed to evaluate safety to bees following a field exposure to spirotetramat at bloom have been conducted in *Phacelia*, melon and citrus. There were no adverse effects to bees or colony health noted in these studies.

These findings suggest an overall favorable environmental package for spirotetramat compared to imidacloprid in pomegranate.

4.6.2 – FIFRA Criterion III: The minor use pesticide plays or will play a significant part in managing pest resistance

There are 163 documented cases of resistance development in cotton aphid, including resistance to IRAC Group 4A insecticides, of which imidacloprid is a member. In addition, there are 98 documented cases of resistance development in greenhouse whitefly, including resistance to imidacloprid (64). To date, no resistance issues have been observed in pomegranate in either of these pests and thus, the registration of spirotetramat on pomegranate, with its excellent efficacy profile (113) will serve to reduce the selection pressure on imidacloprid in this minor-use crop.

4.6.3 - FIFRA Criterion IV: The minor use pesticide plays or will play a significant part in an integrated pest management program

Biological control of aphids is provided by large lady beetles and parasites in the family Aphidiidae. Other important predators include hover flies, green lacewings, predaceous gall midges, and small lady beetles (111). As stated previously, spirotetramat has shown low impact on these naturally-occurring predators and parasites of aphids, allowing both biological and chemical tools to coexist in an IPM program.

4.7 - Pineapple

The key pests infesting pineapple for which spirotetramat has been labeled are mealybugs (114); the pest has also been associated with the disease mealybug wilt of pineapple (115). Table 26 provides a summary of the major alternative insecticides presently registered for control of mealybugs in pineapple. Each of the alternative products listed in Table 26, arranged in order of percent market share from high to low, account for more than 5% of the foliar treated acres.

Table 26. Alternatives to Spirotetramat for Use on Pineapple for Mealybug Control.

Active Ingredient	Brand	IRAC Group	Mode of Action
SPIROTETRAMAT	**MOVENTO**	**23**	**Inhibitor of Acetyl CoA carboxylase**
OXAMYL	VYDATE	1A	Acetylcholinesterase inhibitor
DIAZINON	DIAZINON	1B	Acetylcholinesterase inhibitor
CHLORPYRIFOS	LORSBAN	1B	Acetylcholinesterase inhibitor
PYRIPROXYFEN	KNACK	7C	Juvenile hormone mimic

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

Alternatives Pose Greater Risk to Human Health

Acute toxicity evaluations of the spirotetramat end-use product MOVENTO® and the alternative end-use insecticides are summarized in Table 27 with additional comments below.

Table 27. Comparison of the Toxicity Categories and Signal Words of Spirotetramat End-Use Product with Alternative End-Use Insecticides for Use on Pineapple.

Active Ingredient	Trade Name	Toxicity Category	Signal Word
Spirotetramat	**MOVENTO®**	III	Caution
Chlorpyrifos	Lorsban® 50W	I	Danger
Diazinon	Diazinon 50W	III	Caution
Oxamyl	Vydate® L	I	Danger
Pyriproxyfen	Esteem® 0.86 EC IGR	III	Caution

The spirotetramat end-use product MOVENTO® carries the signal word "Caution" (Category III) based on oral, dermal, and eye irritation hazards. This formulation demonstrates low toxicity by the oral, dermal, and inhalation routes of exposure. Of the four end-use products being compared to spirotetramat in this section, two products have a Category I (Danger) classification and two products have a Category III (Caution) classification. Therefore, two of the four alternative products carry more hazardous acute toxicity classifications than the spirotetramat end-use product MOVENTO®.

Toxicity evaluations of spirotetramat and alternative insecticides are summarized in Table 28 with additional comments below.

Table 28. Active Ingredient Toxicology Summary for Spirotetramat and Major Alternative Insecticides for Use on Pineapple.

Chemical (Technical)	Acute Toxicity	Geno-toxicity	Repro-ductive Toxicity (Primary Evidence)	Develop-mental Toxicity (Primary Evidence)	Onco-genicity Class [c]	Q_1^* (mg/kg/day)$^{-1}$	Chronic Ref Dose (mg/kg/day)
Spirotetramat	**Warning**	–[a]	–	–	**E**	–	**0.132**
Chlorpyrifos	Warning	–	–	–	E	–	0.0003
Diazinon	Caution	–	–	–	E	–	0.0007
Oxamyl	Danger	–	–	+[b]	E	–	0.025
Pyriproxyfen	Caution	–	–	–	E	–	0.35

[a] "-" indicates no evidence within a particular category
[b] "+" indicates positive findings within a category
[c] E: not likely; C: possible; S: suggestive; B2: probable

Spirotetramat, registered by EPA on October 15, 2010, is a new, safer chemistry that will replace organophosphates, neonicotinoids, pyrethroids and other chemistries because of its unique systemicity and broad pest spectrum. Spirotetramat, as well as the alternative products used in pineapple, showed no evidence of oncogenicity in any of the studies conducted in the rat and mouse and is therefore, classified as *not likely to be carcinogenic to humans (Class E).*

The reproductive and prenatal developmental toxicity studies in rats and rabbits provided no evidence to suggest that spirotetramat possesses either a teratogenic or primary toxicological potential, as non-maternal toxicity was identified at equivalent or higher doses than maternal toxicity in both species. Of the products being compared to spirotetramat with toxicological profiles suggestive of a primary toxicological potential, oxamyl showed positive evidence of developmental toxicity.

Based on specific neurotoxicity screening assessments conducted acutely in the rat and incorporated as a satellite investigation as part of the 1-year chronic rat study, spirotetramat did not provide any qualitative or quantitative evidence of a neurotoxic potential. In addition to the specific neurotoxicity testing, no treatment-related clinical signs, changes in absolute brain weight, neuropathological, or neurobehavioral findings were noted in the general toxicity studies (i.e. acute, subacute, subchronic, developmental, reproduction, and chronic). Of the products being compared to spirotetramat in this section, three of the actives, unlike spirotetramat, have cholinesterase inhibiting properties (chlorpyrifos, diazinon, and oxamyl) and one active showed evidence of inducing neurological toxicity (chlorpyrifos).

In vivo and *in vitro* mutagenicity studies with spirotetramat and its metabolites indicate that spirotetramat is not mutagenic – the same is true for the compared alternative products.

The chronic population adjusted dose (cPAD) for spirotetramat is based on the repeated dose 1-year oral toxicity study in the dog, which established a NOAEL of 6 mg/kg bw/day (males). Applying a 100-fold uncertainty factor, the cPAD is 0.06 mg/kg bw/day. Of the products that are being compared to spirotetramat in this section, only pyriproxyfen (0.35 mg/kg/day) has a cPAD greater than spirotetramat, with many of the cPADs being orders of magnitude lower than spirotetramat.

These data suggest an overall favorable toxicology package for spirotetramat compared to the alternative products used in pineapple.

Alternatives Pose Greater Risk to the Environment

Risk assessments demonstrate that spirotetramat 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 29 is a comparison based on Tier 1 risk quotients taken from the reduced risk submissions in which quantitative values of these risk quotients are provided.

Table 29. Summary of Ecological Risk for Spirotetramat and Major Alternative Products for Use on Pineapple.

Chemical	Avian Acute	Avian Chronic	Mammal Acute	Mammal Chronic	Fish Acute	Fish Chronic	Daphnia Acute	Daphnia Chronic	Marine Acute	Bees[1]
Spirotetramat	0.01	2.43	0.02	0.45	<0.01	<0.01	<0.01	<0.01	<0.01	>100
Chlorpyrifos	9.59	52.15	5.83	1131.11	26.76	18.90	481.67	609.60	1376.20	0.059[2]
Diazinon	19.04	202.31	1.44	1456.87	0.57	<32.31	64.25	104.55	12.24	0.22
Oxamyl	4.10	139.29	241.69	24.17	0.01	0.02	0.06	0.01	<0.01	0.31
Pyriproxyfen	<0.01	0.08	<0.01	0.23	<0.01	0.10	0.03	42.96	0.02	>100

No Tier 1 LOC exceedances, or for honey bees, practically non-toxic

Between the endangered species LOC and the high risk LOC for acute risk. Between 1 and 5 times the LOC for chronic risk or for honey bees, moderately toxic.

Greater than the high risk LOC for acute risk. Greater than 5X the LOC for chronic risk. Highly toxic to honey bees.

[1]The "Bees" column gives the 48 h contact LD50 value since there is no EPA risk paradigm for bees with the color indicative of the hazard classification as noted above.
[2] Toxicity after 24 hours

On an acre for acre replacement, the use of spirotetramat reduces the amount of active ingredient applied when compared to most alternative products. Of the five alternative products discussed in this section, only one compound (pyriproxyfen) has lower maximum season application rates. The remaining alternative insecticides from the organophosphate and carbamate classes have much higher seasonal application rates than spirotetramat.

In addition to low application rates, spirotetramat can reduce the environmental burden associated with retreatment of resurgent pest populations. This is possible because of two other unique properties of spirotetramat: (1) systemic movement allows control of pest infestations hidden in dense crop canopies and (2) reduced fecundity of adult female insects extends residual control into the next pest generation.

The estimated ground water concentration for spirotetramat is negligible (i.e., consumes zero percent of the cPAD). This is true even after considering the combined residues of spirotetramat and its degradates. Spirotetramat degrades rapidly in soil and water, leading to low estimated concentrations in aquatic environments. Human exposure to spirotetramat residues in water is anticipated to be negligible consuming 0% of the cPAD for all population subgroups. By comparison, estimated drinking water concentrations consume most or all of the cPAD for many of the alternatives. Therefore, among the alternative compounds, only spirotetramat is expected to have low surface water as well as low ground water contamination risks.

Spirotetramat has minimal acute, adult risk to bees (LD_{50} >100 µg a.i./bee; practically non-toxic). For pineapple uses, spirotetramat compares very favorably to alternative products and is among the least toxic insecticides to honeybees. Spirotetramat and pyriproxyfen are characterized as "practically non-toxic" to honey bees – the remaining alternative insecticides are characterized as "highly toxic" to bees (contact LD_{50} <1 µg/bee).

Bayer CropScience has conducted a comprehensive honey bee safety research and evaluation program. Field studies designed to evaluate safety to bees following a field exposure to spirotetramat at bloom have been conducted in *Phacelia*, melon and citrus. There were no adverse effects to bees or colony health noted in these studies.

These findings suggest an overall favorable environmental package for spirotetramat relative to alternative products used in pineapple.

4.7.2 – FIFRA Criterion III: The minor use pesticide plays or will play a significant part in managing pest resistance

Although no resistance to chemical tools have been reported in the mealybug species infesting pineapple, very limited modes of action exist to control the pest, as evidenced in Table 26, and allow for sufficient rotation for resistance management strategies to be employed. Spirotetramat adds an alternative mode of action to reduce selection pressure on other modes of action currently in this market.

4.7.3 - FIFRA Criterion IV: The minor use pesticide plays or will play a significant part in an integrated pest management program

An effective ant control program makes it possible for the mealybug to be kept under control by predation by natural enemies. Natural predators of the mealybugs have been introduced and are well established. With control of the ants, these natural predators keep the mealybug population in check and reduce disease pressure. However, without elimination of the ants, natural predators are an ineffective control of the mealybugs. Most all insecticide applications are based upon IPM programs. Applications are not made unless the field has had a history of problems or the growing conditions favor insect development. Some growers employ threshold levels to treat (112). As discussed in the introductory sections of this document, spirotetramat has low impact on predators and parasites found in many cropping systems while providing high levels of efficacy against mealybugs infesting pineapple (116).

4.8 - Coffee

The key pest infesting coffee for which spirotetramat has been labeled is green scale. Table 30 provides a summary of the major alternative insecticides presently registered for control of green scale in coffee.

Table 30. Alternative to Spirotetramat for Use on Coffee for Green Scale Control.

Active Ingredient	Brand	IRAC Group	Mode of Action
SPIROTETRAMAT	**MOVENTO**	**23**	**Inhibitor of Acetyl CoA carboxylase**
IMIDACLOPRID	ADMIRE PRO	4A	Nicotinic acetylcholine receptor agonist

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

Alternatives Pose Greater Risk to Human Health

Acute toxicity evaluations of the spirotetramat end-use product MOVENTO® and the alternative end-use insecticide are summarized in Table 31 with additional comments below.

Table 31. Comparison of the Toxicity Categories and Signal Words of Spirotetramat End-Use Product with the Alternative End-Use Insecticide for Use on Coffee.

Active Ingredient	Trade Name	Toxicity Category	Signal Word
Spirotetramat	**MOVENTO®**	III	Caution
Imidacloprid	Admire® Pro	III	Caution

The MOVENTO® end-use product of spirotetramat carries the signal word "Caution" (Category III) based on oral, dermal, and eye irritation hazards. This formulation demonstrates low toxicity by the oral, dermal, and inhalation routes of exposure. The alternative product also carries the signal word "Caution" classification.

Toxicity evaluations of spirotetramat and the alternative insecticide are summarized in Table 32 with additional comments below.

Table 32. Active Ingredient Toxicology Summary for Spirotetramat and the Alternative Insecticide for Use on Coffee.

Chemical (Technical)	Acute Toxicity	Geno-toxicity	Repro-ductive Toxicity (Primary Evidence)	Develop-mental Toxicity (Primary Evidence)	Onco-genicity Class[c]	Q_1^* (mg/kg/day)$^{-1}$	Chronic Ref Dose (mg/kg/day)
Spirotetramat	**Warning**	–[a]	–	–	**E**	–	**0.132**
Imidacloprid	Warning	+/-[b]	–	–	E	–	0.057

[a] "-" indicates no evidence within a particular category
[b] "+/-" indicates positive and negative findings were observed
[c] E: not likely; C: possible; S: suggestive; B2: probable

Spirotetramat, registered by EPA on October 15, 2010, is a new, safer chemistry that will replace organophosphates, neonicotinoids, pyrethroids and other chemistries because of its unique systemicity and broad pest spectrum. Spirotetramat showed no evidence of oncogenicity in any of the studies conducted in the rat and mouse and is therefore, classified as *not likely to be carcinogenic to humans (Class E)*. Imidacloprid is also classified as *not likely to be carcinogenic in humans* (Class E).

The reproductive and prenatal developmental toxicity studies in rats and rabbits provided no evidence to suggest that spirotetramat possesses either a teratogenic or primary toxicological potential, as non-maternal toxicity was identified at equivalent or higher doses than maternal toxicity in both species.

Based on specific neurotoxicity screening assessments conducted acutely in the rat and incorporated as a satellite investigation as part of the 1-year chronic rat study, spirotetramat did not provide any qualitative or quantitative evidence of a neurotoxic potential. In addition to the specific neurotoxicity testing, no treatment-related clinical signs, changes in absolute brain weight, neuropathological, or neurobehavioral findings were noted in the general toxicity studies (i.e. acute, subacute, subchronic,

developmental, reproduction, and chronic). Imidacloprid showed evidence of inducing neurological toxicity.

In vivo and *in vitro* mutagenicity studies with spirotetramat and its metabolites indicate that spirotetramat is not mutagenic. Imidacloprid showed some evidence of positive responses (*in vivo* and/or *in vitro*) in gene mutational testing or cytogenetic testing.

The comparison to imidacloprid suggests an overall more favorable toxicology package for spirotetramat.

Alternatives Pose Greater Risk to the Environment

Risk assessments demonstrate that spirotetramat 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 33 is a comparison based on Tier 1 risk quotients taken from the reduced risk submissions in which quantitative values of these risk quotients are provided.

Table 33. Summary of Ecological Risk for Spirotetramat and the Alternative Product for Use on Coffee.

Chemical	Avian Acute	Avian Chronic	Mammal Acute	Mammal Chronic	Fish Acute	Fish Chronic	Daphnia Acute	Daphnia Chronic	Marine Acute	Bees[1]
Spirotetramat	0.01	2.43	0.02	0.45	<0.01	<0.01	<0.01	<0.01	<0.01	>100
Imidacloprid	0.07	2.32	0.11	2.63	<0.01	<0.01	<0.01	<0.01	0.17	0.04

No Tier 1 LOC exceedances, or for honey bees, practically non-toxic

Between the endangered species LOC and the high risk LOC for acute risk. Between 1 and 5 times the LOC for chronic risk or for honey bees, moderately toxic.

Greater than the high risk LOC for acute risk. Greater than 5X the LOC for chronic risk. Highly toxic to honey bees.

[1]The "Bees" column gives the 48 h contact LD50 value since there is no EPA risk paradigm for bees with the color indicative of the hazard classification as noted above.

On an acre for acre replacement, the use of spirotetramat reduces the amount of active ingredient applied when compared to imidacloprid on a seasonal basis. This is possible because of two other unique properties of spirotetramat: (1) systemic movement allows control of pest infestations hidden in dense crop canopies and (2) reduced fecundity of adult female insects extends residual control into the next pest generation.

The estimated ground water concentration for spirotetramat is negligible (i.e., consumes zero percent of the cPAD). This is true even after considering the combined residues of spirotetramat and its degradates. Spirotetramat degrades rapidly in soil and water, leading to low estimated concentrations in aquatic environments. Human exposure to spirotetramat residues in water is anticipated to be negligible consuming 0% of the cPAD for all population subgroups. Spirotetramat is expected to have low surface water as well as low ground water contamination risks.

Spirotetramat has minimal acute, adult risk to bees (LD_{50} >100 µg a.i./bee; practically non-toxic). Conversely, imidacloprid is characterized as "highly toxic" to bees (contact LD_{50} <1 µg/bee).

Bayer CropScience has conducted a comprehensive honey bee safety research and evaluation program. Field studies designed to evaluate safety to bees following a field exposure to spirotetramat at bloom have been conducted in *Phacelia*, melon and citrus. There were no adverse effects to bees or colony health noted in these studies.

These findings suggest an overall favorable environmental package for spirotetramat compared to imidacloprid in coffee.

4.8.2 – FIFRA Criterion III: The minor use pesticide plays or will play a significant part in managing pest resistance

There are no documented cases of resistance development in green scale infesting coffee, to date. However, having only a single mode of action for control of this pest places extreme selection pressure on the population. Spirotetramat has shown good control of green scale in limited testing (117, 118) and its registration on coffee brings an additional mode of action to reduce selection pressure to the neonicotinoid chemistry. However, additional modes of action over and above spirotetramat and imidacloprid are needed soon.

4.8.3 - FIFRA Criterion IV: The minor use pesticide plays or will play a significant part in an integrated pest management program

Due to lack of available information, it is unknown about current IPM practices in coffee. However, in other crops, various species of scales are affected by naturally occurring predators and parasitoids and the use of spirotetramat would have minimal impact on those species which would foster IPM in coffee production.

Conclusions

The 53 spirotetramat minor uses identified above satisfy several of the criteria for granting the three-year extension of exclusive use data protection as provided under FIFRA Section 3(c)(1)(F)(ii). Residue data have been submitted for each of these 53 minor use crops. These 53 qualifying minor uses registered for spirotetramat greatly exceed the nine minor uses required for an additional three years of exclusive use. Spirotetramat is an extremely valuable tool for control of aphids, mealybugs, psyllids, scales, certain thrips species, and whiteflies and offers suppressive effects against other insect and nematode pests.

Spirotetramat brings a new insecticidal mode of action to a wide range of crops and target insect pests. It will improve the adoption of integrated pest management strategies by providing a much needed resistance management tool, introducing a new product with a favorable human and ecological risk profile and extending the life of other resistance management pesticides. Spirotetramat is highly efficacious at low doses; most of the alternative products have application rates higher than spirotetramat, many of them by an order of magnitude or more. Spirotetramat's low use rate coupled with its unique systemic activity and residual control will result in fewer insecticide applications and a lower overall environmental burden.

Spirotetramat reduces the risk of pesticides to human health by reducing the use of Category I cholinesterase inhibiting insecticides such as the OPs, class C carcinogens, and developmental and reproductive toxicants.

Spirotetramat reduces the risk of pesticides to non-target organisms. A comparison of risk quotients demonstrates that overall, spirotetramat poses less risk to non-target organisms than many of the alternative products. Many of the alternative products have risk quotients several orders of magnitude larger than spirotetramat.

Spirotetramat reduces the potential for contamination of groundwater and surface water. Most of the alternative products have application rates higher than spirotetramat, many of them having rates an order of magnitude or more higher than spirotetramat. The calculated groundwater screening concentration for spirotetramat is less than 0.01% of the cPAD, and is a lower percent of the cPAD than any of the alternative products with some of the alternative values being orders of magnitude higher than spirotetramat. Similar results were obtained when estimated drinking water concentrations from surface water are considered with the spirotetramat concentration being the lowest percent of the cPAD and many of the alternatives having values many orders of magnitude higher.

Bayer CropScience believes that spirotetramat exceeds the statutory minimum number of required minor use registrations and meets several of the criteria required for extending the exclusive use period by the statutory maximum of three years. Based on the current exclusive use expiration date for spirotetramat of February 4, 2019, we would request a revised exclusive use expiration date of February 4, 2022. We look forward to receiving EPA's decision on this petition and confirming the additional three years of exclusive use data protection for spirotetramat under FIFRA Section 3(c)(1)(F)(ii).

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