UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

WASHINGTON, D.C. 20460

OFFICE OF
PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

MEMORANDUM

Date: 17-APR-2008

Subject: **Spirotetramat:** Summary of Analytical Chemistry and Residue Data for Setting Tolerances in/on Citrus (Crop Group 10); Cucurbit Vegetables (Crop Group 9); Fruiting Vegetables (Crop Group 8); Grape (Crop Subgroup 13F); Hops; Leafy *Brassica* Vegetables (Crop Group 5); Leafy Non-*Brassica* Vegetables (Crop Group 4); Pome Fruit (Crop Group 11); Potato and Other Tuberous and Corm Vegetables (Crop Subgroup 1C); Stone Fruit (Crop Group 12); Tree Nuts (Crop Group 14); Onions; Strawberries; and Livestock Commodities. Decision No. 371317; 40 CFR 180.xxx.

PC Code: 392201
MRID Nos.: 46904479-99, 46904501-26, 47151101-05, 47180401-02, 47281301-07, 47291201, 47143501-02, 47208001
Petition No.: 6F7119
Assessment Type: None
TXR No.: None

DP No.: 339694
Registration Nos.: 264-xxx

Regulatory Action: Section 3 Registration
Reregistration Case No.: None
CAS No.: 382608-10-8

From: George F. Kramer, Ph.D., Senior Chemist
Registration Action Branch 1 (RAB1)
Health Effects Division (HED) (7509P)

Through: Dana M. Vogel, Branch Chief
RAB1/HED (7509P)

To: Rita Kumar/Meredith Laws, PM Team 01
Registration Division (RD; 7505P)

Executive Summary

Spirotetramat is a tetramic acid derivative (ketoenole) developed by Bayer CropScience AG. This foliar insecticide is active against sucking insects in vegetables, citrus, pome fruit, stone fruit, grapes, cotton and other plants. It is systemic (xylem and phloem mobile) and can control hidden pests and protect new shoots. There are currently no registrations for spirotetramat in the U.S. Spirotetramat is being evaluated as part of a trilateral joint review with Canada and Austria.

Bayer CropScience has submitted a Section 3 request to register a 2 lb a.i./gal suspension-concentrate (SC) formulation (Movento™; EPA Reg. No. 264-xxx), a 1.25 lb a.i./gal SC formulation (Ultor™; EPA Reg. No. 264-xxx), and a 1.25 lb a.i./gal oil-dispersion (OD) formulation (BYI 8330 OD; EPA Reg. No. 264-xxx) for use on citrus, cucurbit vegetables, fruiting vegetables, grapes, hops, leafy *Brassica* vegetables, leafy non-*Brassica* vegetables, pome fruit, tuberous and corm vegetables, stone fruit, and tree nuts. This registration request represents the first food use for the insecticide. The end-use products are proposed for 2-4 foliar spray applications at 0.05-0.16 lb a.i./A/application with a minimum retreatment intervals (RTIs) of 7-30 days, for maximum seasonal rates of 0.16-0.40 lb a.i./A. Applications may be made using ground or aerial equipment, and use of an adjuvant is required. Preharvest intervals (PHIs) of 1-7 days are proposed.

Concurrently, Bayer CropScience has submitted a petition for the establishment of permanent tolerances for residues of spirotetramat (cis-3-(2,5-dimethlyphenyl)-8-methoxy-2-oxo-1-azaspiro[4.5]dec-3-en-4-yl-ethyl carbonate]) and its metabolite BYI 08330-enol (cis-3-(2,5-dimethylphenyl)-4-hydroxy-8-methoxy-1-azaspiro[4.5]dec-3-en-2-one), calculated as spirotetramat equivalents, in/on the following commodities:

Citrus, Crop group 10	0.5 ppm
Citrus, oil	4 ppm
Leafy Vegetables, Crop group 4	5 ppm
Pome Fruit, Crop group 11	0.5 ppm
Apple, wet pomace	0.6 ppm
Stone Fruit, Crop group 12	2 ppm
Grape, wine and table grape, Crop Group 13F	1 ppm
Grapes, raisins	2.5 ppm
Strawberry	0.5 ppm
Bulb Vegetables, Onion, Crop Group 3A	0.3 ppm
Fruiting Vegetables, Crop group 8	1 ppm
Tomato, dried	2.5 ppm
Cucurbits, Crop Group 9	0.2 ppm
Brassica, Head and Stem, Crop group, Crop Group 5A	1 ppm
Leafy *Brassica*, Crop Group 5B	16 ppm
Potato, Crop Group 1C	1 ppm
Potato, flakes	2.5 ppm
Tree Nuts, Crop Group 14	0.5 ppm
Almond, hulls	9 ppm
Hop (dried cones)	10 ppm
Cattle, meat	0.01 ppm
Cattle, fat	0.01 ppm
Cattle, liver	0.01 ppm
Cattle, meat byproducts, except liver	0.02 ppm
Goat, meat	0.01 ppm
Goat, fat	0.01 ppm
Goat, liver	0.01 ppm
Goat, meat byproducts, except liver	0.02 ppm
Hog, meat	0.01 ppm
Hog, fat	0.01 ppm

Hog, liver	0.01 ppm
Hog, meat byproducts, except liver	0.02 ppm
Sheep, meat	0.01 ppm
Sheep, fat	0.01 ppm
Sheep, liver	0.01 ppm
Sheep, meat byproducts, except liver	0.02 ppm
Horse, meat	0.01 ppm
Horse, fat	0.01 ppm
Horse, liver	0.01 ppm
Horse, meat byproducts, except liver	0.02 ppm

The nature of the residue in plants, rotational crops, and livestock is adequately understood based on acceptable metabolism studies conducted on apple, lettuce, cotton, potato, rotational crops, lactating goats, and laying hens.

In plants, the major metabolic reaction involved the hydrolytic cleavage of the carbonate ester parent bond of the parent compound to form BYI 08330-enol. Further reduction of the double bond in the teramic acid moiety of BYI 08330-enol occurred to form the BYI 08330-mono-hydroxy metabolite. Hydroxylation in the tetramic acid moiety resulted in BYI 08330-ketohydroxy. Demethylation of the methoxy group of the cyclohexyl ring resulted via a proposed intermediate (BYI 08330-desmethyl-enol) in BYI 08330-desmethyl-ketohydroxy (after the corresponding hydroxylation). Oxidation of the methoxy group resulted in BYI 08330-ketohydroxy-formiate. Partly, metabolites bearing a hydroxy group were conjugated with glucose. The residues of concern for the tolerance expression and risk assessment for plant commodities are spirotetramat and its metabolites BYI 08330-enol, BYI 08330-ketohydroxy, BYI08330-enol-Glc, and BYI 08330-mono-hydroxy (Memo, J. Tyler *et al.*, 4/16/08; D333437).

The metabolism of spirotetramat in rotational crops appears to be consistent with the pathway observed in the plant metabolism studies. The residues of concern for rotational crops are spirotetramat and BYI 08330-ketohydroxy and free and conjugated BYI 08330-desmethyl-ketohydroxy, BYI 08330-desmethyl-di-hydroxy and BYI 08330-ketohydroxy-alcohol (Memo, J. Tyler *et al.*, 4/16/08; D333437). Unless the petitioner requests plantback intervals (PBIs) shorter than 30 days, no additional data are required, and tolerances for inadvertent residues in/on rotational crops need not be established in conjunction with the currently proposed uses.

In livestock, the biodegradation of spirotetramat in livestock can be characterized as cleavage of the carbonate ester group to the primary metabolite BYI 08330-enol followed by conjugation of the enol hydroxy group with glucuronic acid to BYI 08330-enol-GA. Oxidation of the azaspirodecenyl moiety to BYI 08330-ketohydroxy and demethylation of the methoxy group to BYI 08330-desmethyl-enol were minor metabolic reactions in ruminants as well as reduction of the azaspirodecenyl moiety to BYI 08330-monohydroxy. Based on the currently proposed uses, the residues of concern for the tolerance expression for livestock commodities are spirotetramat and its metabolite BYI 08330-enol and the residues of concern for the risk assessment for livestock commodities are spirotetramat and its metabolites BYI 08330-enol and BYI 08330-enol-GA (Memo, J. Tyler *et al.*, 4/16/08; D333437). If future proposed uses result in significant exposure of livestock to the plant metabolites BYI 08330-ketohydroxy, BYI08330-enol-Glc, and BYI 08330-mono-hydroxy, then these metabolites may need to be included as additional residues of concern for livestock commodities.

The petitioner has submitted several high-performance liquid chromatography with positive-ion electrospray tandem mass spectrometry (HPLC-MS/MS) residue analytical methods for the determination of residues of the parent and its metabolites in/on plant and livestock commodities. Analytical method 00857 was developed for the determination of residues of spirotetramat, the metabolites BYI 08330-enol, BYI 08330-ketohydroxy, BYI 08330-mono-hydroxy and BYI 08330-enol-Glc in plant matrices by HPLC-MS/MS. The analytical method 00966 was developed for the determination of residues of spirotetramat and the metabolites BYI 08330-enol and BYI 08330-enol-GA in livestock matrices by HPLC-MS/MS. These methods were used as the data-collection methods in the analysis of samples for residues of concern from the various studies associated with the current petition. Each method has been adequately validated by the petitioner as well as by independent laboratories. Methods 00857 and 00966 were also adequately radiovalidated using weathered samples obtained from metabolism studies.

HED has determined that Methods 00857 and 00966 are suitable enforcement methods for plant and livestock commodities, respectively, since the methods passed a successful petition method validation (PMV) by Agency chemists at the Analytical Chemistry Laboratory/Biological and Economics Analysis Division (ACL/BEAD) (E-mail, C. Stafford to D. Vogel; 2/19/08).

The submitted magnitude of the residue data for the raw agricultural commodities (RACs) of citrus, cucurbit vegetables, fruiting vegetables, grapes, hops, leafy *Brassica* vegetables, leafy non-*Brassica* vegetables, pome fruit, tuberous and corm vegetables, stone fruit, and tree nuts and the European residue for strawberries and onions data are adequate. There are adequate storage stability data to validate the storage conditions and intervals of samples collected from the field trials.

Acceptable apple, orange, grape, plum, potato, and tomato processing studies are available. The processing studies show that following processing of RAC samples bearing quantifiable residues, total residues of spirotetramat and its metabolites concentrated in apple wet pomace (1.9X), citrus oil (13.5X), raisins (2.6X), prunes (2.2X), potato flakes (3.5X), potato chips (1.2X), tomato paste (7.4X) and tomato purée (3.5X).

An adequate dairy cow feeding study has been submitted; this study is acceptable for determining tolerance levels for livestock commodities. Based on the submitted data, HED has concluded that the tolerances, expressed as spirotetramat and its metabolite BYI 08330-enol, are required for some for livestock commodities. As none of the proposed target crops are considered as a commodity for poultry feed, data depicting residues in laying hens are not required.

Regulatory Recommendations and Residue Chemistry Deficiencies

Pending submission of a revised Sections B and F (see requirements under Directions for Use and Proposed Tolerances) and the submission of reference standards for the spirotetramat metabolites (see requirements under Submittal of Analytical Reference Standards); there are no residue chemistry issues that would preclude granting an unconditional registration for the use of spirotetramat on the requested crops.

The proposed uses and the submitted data support the following permanent tolerances for the combined residues of spirotetramat (cis-3-(2,5-dimethlyphenyl)-8-methoxy-2-oxo-1-azaspiro[4.5]dec-3-en-4-yl-ethyl carbonate]) and its metabolites BYI 08330-enol (cis-3-(2,5-

dimethylphenyl)-4-hydroxy-8-methoxy-1-azaspiro[4.5]dec-3-en-2-one), BYI 08330-ketohydroxy (cis-3-(2,5-dimethylphenyl)-3-hydroxy-8-methoxy-1-azaspiro[4.5]decane-2,4-dione), BYI08330-enol-Glc (cis-3-(2,5-dimethylphenyl)-8-methoxy-2-oxo-1-azaspiro[4.5]dec-3-en-4-yl beta-D-glucopyranoside), and BYI 08330-mono-hydroxy (cis-3-(2,5-dimethylphenyl)-4-hydroxy-8-methoxy-1-azaspiro[4.5]decan-2-one), calculated as spirotetramat equivalents, in/on the following commodities:

Fruit, citrus, group 10	0.60 ppm	Vegetable, fruiting, group 8	2.5 ppm
Citrus, oil	6.0 ppm	Vegetable, cucurbit, group 9	0.30 ppm
Vegetable, leafy, except *Brassica,* group 4	9.0 ppm	*Brassica*, head and stem, subgroup 5A	2.5 ppm
Fruit, pome, group 11	0.70 ppm	*Brassica*, leafy greens, subgroup 5B	8.0 ppm
Fruit, stone, group 12	4.5 ppm	Vegetable, tuberous and corm, subgroup 1C	0.60 ppm
Small fruit vine climbing subgroup, except fuzzy kiwifruit, subgroup 13-07F	1.3 ppm	Potato, flakes	1.6 ppm
Grape, raisin	3.0 ppm	Nut, tree, group 14	0.25 ppm
Strawberry	0.40 ppm	Almond, hulls	9.0 ppm
Onion, bulb, subgroup 3A-07	0.30 ppm	Hop, dried cones	10 ppm
Okra	2.5 ppm		

The proposed uses and the submitted data support the following tolerances for the combined residues of spirotetramat (cis-3-(2,5-dimethlyphenyl)-8-methoxy-2-oxo-1-azaspiro[4.5]dec-3-en-4-yl-ethyl carbonate]) and its metabolite BYI 08330-enol (cis-3-(2,5-dimethylphenyl)-4-hydroxy-8-methoxy-1-azaspiro[4.5]dec-3-en-2-one), calculated as spirotetramat equivalents, in/on the following livestock commodities:

Milk	0.01 ppm	Sheep, meat	0.02 ppm
Cattle, meat	0.02 ppm	Sheep, fat	0.02 ppm
Cattle, fat	0.02 ppm	Sheep, meat byproducts	0.02 ppm
Cattle, meat byproducts	0.02 ppm	Horse, meat	0.02 ppm
Goat, meat	0.02 ppm	Horse, fat	0.02 ppm
Goat, fat	0.02 ppm	Horse, meat byproducts	0.02 ppm
Goat, meat byproducts	0.02 ppm		

860.1200 Directions for Use

- The labels should be amended to specify a 30-day PBI for all non-labeled crops.

860.1650 Submittal of Analytical Reference Standards

- Analytical standards for the metabolites of spirotetramat are currently not available in the National Pesticide Standards Repository [Source: personal communication with D. Wright Jr. of ACL/BEAD, 11/2/2007]. Analytical reference standards (both technical-grade and isotopically labeled) of BYI 08330-enol, BYI 08330-ketohydroxy, BYI 08330-mono-hydroxy, and BYI 08330-enol-Glc should be supplied, and supplies replenished as requested by the Repository.

860.1550 Proposed Tolerances

The petitioner is requested to submit a revised Section F specifying the following:

- The tolerance expression for plant commodities should be revised to include the combined residues of spirotetramat and its metabolites BYI 08330-enol, BYI 08330-ketohydroxy, BYI08330-enol-Glc, and BYI 08330-mono-hydroxy, expressed as spirotetramat equivalents.

- Revised tolerance levels and commodity definitions presented in Table 49 (summarized above).

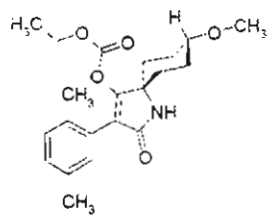
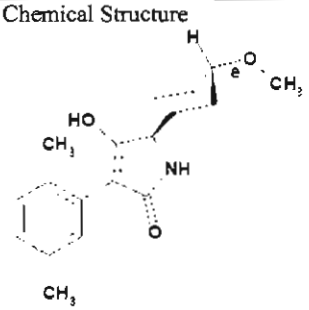
A human-health risk assessment is forthcoming.

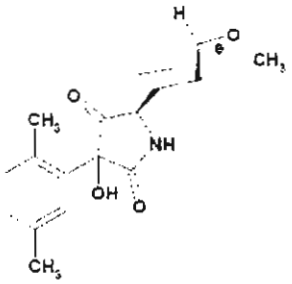
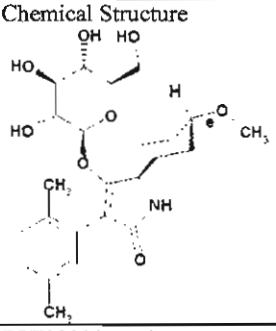
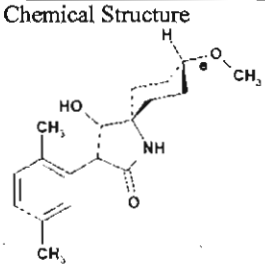
Background

Spirotetramat is a tetramic acid derivative (ketoenole) developed by Bayer CropScience AG. This foliar insecticide is active against sucking insects in vegetables, citrus, pome fruit, stone fruit, grapes, cotton and other plants. It is systemic (xylem and phloem mobile) and can control hidden pests and protect new shoots.

Details of the test compound nomenclature for spirotetramat and its metabolites BYI 08330-enol, BYI 08330-ketohydroxy, BYI 08330-mono-hydroxy, BYI 08330-enol-GA, and BYI 08330-enol-Glc are presented in Table 1. The physicochemical properties of technical grade spirotetramat are listed in Table 2. The chemical names and structures of spirotetramat and its transformation products are presented in Appendix I.

Table 1. Test Compound Nomenclature.

Compound	Chemical Structure 
Common name	Spirotetramat
Company experimental name	BYI 08330
IUPAC name	*cis*-4-(ethoxycarbonyloxy)-8-methoxy-3-(2,5-xylyl)-1-azaspiro[4.5]dec-3-en-2-one
CAS name	*cis*-3-(2,5-dimethylphenyl)-8-methoxy-2-oxo-1-azaspiro[4.5]dec-3-en-4-yl ethyl carbonate
CAS #	382608-10-8
End-use product/EP	Movento™, Ultor™, BYI 8330 OD
Compound: BYI08330-enol	Chemical Structure 
Common name	BYI08330-enol
Company experimental name	BYI08330-enol

IUPAC name	None provided
CAS name	*cis*-3-(2,5-dimethylphenyl)-4-hydroxy-8-methoxy-1-azaspiro[4.5]dec-3-en-2-one
CAS #	None provided
Compound: BYI08830-ketohydroxy	Chemical Structure 
Common name	BYI08830-ketohydroxy
Company experimental name	BYI08830-ketohydroxy
IUPAC name	None provided
CAS name	*cis*-3-(2,5-dimethylphenyl)-3-hydroxy-8-methoxy-1-azaspiro[4.5]decane-2,4-dione
CAS #	None provided
Compound: BYI08330-enol-Glc	Chemical Structure 
Common name	BYI08330-enol-Glc
Company experimental name	BYI08330-enol-Glc
IUPAC name	None provided
CAS name	*cis*-3-(2,5-dimethylphenyl)-8-methoxy-2-oxo-1-azaspiro[4.5]dec-3-en-4-yl beta-D-glucopyranoside
CAS #	None provided
Compound: BYI 08330-mono-hydroxy	Chemical Structure 
Common name	BYI 08330-mono-hydroxy
Company experimental name	BYI 08330-mono-hydroxy
IUPAC name	None provided
CAS name	*cis*-3-(2,5-dimethylphenyl)-4-hydroxy-8-methoxy-1-azaspiro[4.5]decan-2-one
CAS #	None provided
Compound: BYI 08330-enol-GA	Chemical Structure

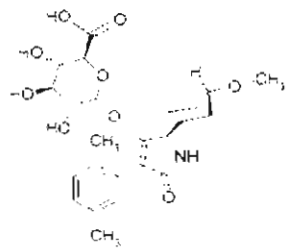
	
Common name	BYI 08330-enol-GA
Company experimental name	BYI 08330-enol-GA
IUPAC name	None provided
CAS name	*cis*-3-(2,5-dimethylphenyl)-4-(β-D-glucopyranosyloxy)-8-methoxy-1-azaspiro[4.5]dec-3-en-2-one
CAS #	None provided

Table 2. Physicochemical Properties of the Technical Grade Spirotetramat.

Parameter	Value	Reference
Melting Point (°C)	142	Bayer CropScience AG Report M-063268-01-1
pH	6.3	Bayer CropScience AG Report M-269907-01-1
Density	$D_4^{20} = 1.22$	Bayer CropScience AG Report M-270041-01-1
Solubility in water at 20°C	pH 4 - 33.5 mg/L pH 7 - 29.9 mg/L pH9 - 19.1 mg/L	Bayer CropScience AG Report M-103256-01-1
Solubility in organic solvent at 20°C	Solvent — g/L n-hexane — 0.055 Dichloromethane — >600 Dimethyl Sulfoxide — 200-300 Toluene — 60 Acetone — 100–120 Ethyl acetate — 67 Ethanol — 44	Bayer CropScience AG Report M-122802-01-1
Partition Coefficient n-octanol/water (log K_{ow})	pH 4 - 2.51 pH 7 - 2.51 pH 9 - 2.50	Bayer CropScience AG Report M-103244-01-1
Vapor pressure (Pa)	Extrapolated Values: 5.6×10^{-9} (20°C) 1.5×10^{-8} (25°C) 1.5×10^{-6} (50°C)	Bayer CropScience AG Report M-066171-01-1
UV/Visible Absorption Spectra	Peak Maxima (nm) — Molar Absorptivity (1000 cm^2/ mol) 211 — 22.0×10^3 276 — 0.8×10^3	Bayer CropScience AG M-182543-02-1

860.1200 Directions for Use

The petitioner has submitted draft labels dated 10/5/07 for the 2 lb a.i./gal SC formulation (Movento™; EPA Reg. No. 264-xxx), for the 1.25 lb a.i./gal SC formulation (Ultor™; EPA Reg. No. 264-xxx),and the 1.25 lb a.i./gal OD formulation (BYI 8330 OD; EPA Reg. No. 264-xxx). Information pertaining to the proposed end-use product is listed in Table 3. A summary of the proposed use patterns on citrus, cucurbit vegetables, fruiting vegetables, grapes, hops, leafy *Brassica* vegetables, leafy non-*Brassica* vegetables, pome fruit, tuberous and corm vegetables, stone fruit, and tree nuts is detailed in Table 4.

Table 3. Summary of Proposed End-Use Products.

Trade Name	Reg. No.	a.i. (% of formulation)	Formulation Type	Target Crops	Target Pests	Label Date
Movento™	264-xxx	22.4	SC	citrus, grapes, pome fruit, stone fruit, tree nuts, hops, Christmas tree, vegetables and potato.	sucking insects	Draft labels submitted 10/5/07
Ultor™	264-xxx	14.5	SC			
BYI 8330 OD	264-xxx	15.3	OD			

Table 4. Summary of Directions for Use of Spirotetramat.

Trade Names	Application Timing, Type, and Equipment	Application Rate (lb a.i./A)	Maximum Number Applications per Season	Maximum Seasonal Application Rate (lb a.i./A)	PHI (days)	Use Directions and Limitations
CITRUS (Crop Group 10)						
BYI 8330 OD Movento™ Ultor™	Ground & aerial	0.12-0.16	2	0.32	1	Minimum RTI: 21 days Minimum spray volume: 15 gallons per acre (GPA) ground, 10 GPA aerial
GRAPE and SMALL FRUIT VINE CLIMBING (except kiwifruit)						
BYI 8330 OD Movento™ Ultor™	Ground & aerial	0.08-0.12	2	0.20	7	Minimum RTI: 30 days Minimum spray volume: 15 GPA ground, 10 GPA aerial
POME FRUIT (Crop Group 11)						
BYI 8330 OD Movento™ Ultor™	Ground & aerial	0.10-0.14	4	0.40	7	Minimum RTI: 14 days Minimum spray volume: 15 GPA ground, 10 GPA aerial
STONE FRUIT (Crop Group 12)						
BYI 8330 OD Movento™ Ultor™	Ground & aerial	0.10-0.14	2	0.24	7	Minimum RTI: 14 days Minimum spray volume: 15 GPA ground, 10 GPA aerial
TREE NUTS (Crop Group 14)						
BYI 8330 OD Movento™ Ultor™	Ground & aerial	0.10-0.14	3	0.34	7	Minimum RTI: 14 days Minimum spray volume: 15 GPA ground, 10 GPA aerial
HOPS						
BYI 8330 OD Movento™ Ultor™	Ground & aerial	0.08-0.10	2	0.20	7	Minimum RTI: 14 days Minimum spray volume: 10 GPA ground, 10 GPA aerial
CUCURBIT VEGETABLES (Crop Group 9)						
BYI 8330 OD Movento™ Ultor™	Ground, chemigation, & aerial	0.05-0.08	3	0.16	1	Minimum RTI: 7 days Minimum spray volume: 15 GPA ground, 5 GPA aerial
FRUITING VEGETABLES (Crop Group 8) + OKRA						
BYI 8330 OD Movento™ Ultor™	Ground, chemigation, & aerial	0.05-0.08	3	0.16	1	Minimum RTI: 7 days Minimum spray volume: 15 GPA ground, 5 GPA aerial
LEAFY VEGETABLES - NON-*BRASSICA* (Crop Group 4)						
BYI 8330 OD Movento™ Ultor™	Ground, chemigation, & aerial	0.05-0.08	3	0.16	3	Minimum RTI: 7 days Minimum spray volume: 15 GPA ground, 5 GPA aerial
BRASSICA (COLE) LEAFY VEGETABLES (Crop Group 5)						
BYI 8330 OD	Ground, chemigation,	0.05-0.08	3	0.16	1	Minimum RTI: 7 days

Table 4. Summary of Directions for Use of Spirotetramat.

Trade Names	Application Timing, Type, and Equipment	Application Rate (lb a.i./A)	Maximum Number Applications per Season	Maximum Seasonal Application Rate (lb a.i./A)	PHI (days)	Use Directions and Limitations
Movento™ Ultor™	& aerial					Minimum spray volume: 15 GPA ground, 5 GPA aerial
POTATO and OTHER TUBEROUS AND CORM VEGETABLES (Crop Group 1C)						
BYI 8330 OD Movento™ Ultor™	Ground, chemigation, & aerial	0.06-0.08	2	0.16	7	Minimum RTI: 7 days Minimum spray volume: 15 GPA ground, 5 GPA aerial
Additional Restrictions for all Crops:						
MOVENTO™ and Ultor™ must be tank-mixed with a spray adjuvant/additive. BYI 8330 OD may be tank-mixed with a spray adjuvant/additive. Use in enclosed structures, such as greenhouses or planthouses, is not permitted unless specified otherwise by state-specific supplemental labeling. Rotational PBIs: Immediate plant-back: All crops						

Conclusions. The submitted use directions for Movento™, Ultor™, BYI 8330 OD are adequate to allow evaluation of the residue data relative to the proposed use. The specified rotational PBIs allow immediate plantback of all crops. However, the rotational crop data support a rotational crop restriction of 30 days for all non-labeled crops. The labels should thus be amended to specify the 30-day PBI.

860.1300 Nature of the Residue - Plants

DER Reference List: 46904480.der.doc (Apple)
46695529.der.doc (Lettuce)
46904479.der.doc (Cotton)
46904484.der.doc (Potato)

Apple

The metabolism of spirotetramat was investigated in apple (fruits & leaves) following two spray applications of [azaspirodecenyl-3-^{14}C]-spirotetramat (100 OD) at a total rate of 1100 g a.i./ha (0.982 lb a.i./A, 2.5X). The first application was at a growth stage 69 of the current BBCH code and the second application was 20 days later at growth stage 71, 2 months (63 days) before harvest.

Total radioactive residue (TRR) amounted to 0.61 ppm (apple) and 36.63 ppm (apple leaves). Approximately 49% of the TRR (0.3 ppm) in apple was surface residues washed with dichloromethane. Washed apple extracted with acetonitrile (ACN)/water yielded 49.5% of the TRR leaving only 2.1% of the TRR (0.01 ppm) as unextractable residues. Unchanged parent spirotetramat was the only residue detected in the surface wash. The predominant residue found in the extract was BYI 08330-mono-hydroxy followed by BYI 08330-ketohydroxy, BYI 08330-di-hydroxy, BYI 08330-desmethyl-ketohydroxy, BYI 08330-enol, and the respective glycosides thereof.

As in apple fruits, the major residue in apple leaves was the unchanged spirotetramat (72% of the TRR). Other residues detected were BYI 08330-ketohydroxy, BYI 08330-enol, and glycoside isomers of BYI 08330-desmethyl-ketohydroxy. A BYI 08330-ketohydroxy-formiate-glycoside

was also detected.

A supplementary apple cell culture study was also submitted. This study was conducted to ascertain the metabolic fate of spirotetramat in isolated plant cells. As well, from this study, selected metabolites were obtained in larger amounts to be used as radioactive reference compounds in guideline nature of the residue studies.

In this study, heterotrophic plant cell suspension cultures originating from apple fruit were incubated with [azaspirodecenyl-3-^{14}C]-spirotetramat. After seven days of incubation, the cells were separated from the nutrient by filtration, and extracted with ACN/water. The cell extract and nutrient medium were partitioned with ethyl acetate. Approximately 44% of the recovered radioactivity was found in the cells and ~ 56% in the nutrient medium. The major part of the radioactivity present in the extracts of cells and nutrient medium partitioned into the organic phase (ethyl acetate). The formation of bound residues observed was minimal (<1% of the recovered radioactivity).

Spirotetramat was rapidly degraded by the apple cells and up to 14 different metabolites were isolated from the organic and aqueous phases of the nutrient media and cell extracts, respectively. Thirteen of these were identified by spectroscopic methods.

Major reactions involved in the degradation of the parent compound were hydrolysis of the side chain carbonate ester bond resulting in the BYI 08330-enol. A second hydroxylation detected in the azaspiro moiety of this BYI 08330-enol gave the BYI 08330-keto-hydroxy. Demethylation of BYI 08330-enol resulted in the corresponding BYI 08330-4-hydroxyenol and further hydroxylation correspondingly in the BYI 08330-hydroxy-keto-hydroxy metabolite. All metabolites were further conjugated to give mono and bis-glycosides.

TABLE 5. Summary of Characterization and Identification of Radioactive Residues in Apple Matrices Following Target Application of Radiolabeled Spirotetramat at 0.982 lb a.i./A (2.5X).

Compound	Apple Fruit TRR = 0.61 ppm		Apple Leaves TRR = 36.63 ppm	
	% TRR	ppm	% TRR	ppm
Spirotetramat (parent)	51.3	0.32	72.0	26.37
BYI 08330-ketohydroxy	7.7	0.05	3.0	1.09
BYI 08330-enol	2.1	0.01	11.6	4.26
BYI 08330-mono-hydroxy	15.6	0.10	ND	ND
BYI 08330-desmethyl-ketohydroxy	3.8	0.02	ND	ND
BYI 08330-di-hydroxy	4.4	0.03	ND	ND
BYI 08330-desmethyl-ketohydroxy-Glc (isomers), in leaves also +BYI 08330-ketohydroxy-formiate-glycoside	1.9	0.01	8.0	2.92
BYI 08330-enol-glycoside	5.1	0.03	ND	ND
Total identified	91.9	0.57	94.6	34.65
Total characterized	6.0	0.04	ND	ND
Total extractable	98.0	0.60	94.6	34.65
Unextractable[1]	2.1	0.01	5.4	1.97

[1] Residues remaining after exhaustive extractions.

Lettuce

The metabolism of spirotetramat was investigated in head lettuce following two spray applications of [azaspirodecenyl-3-^{14}C]-spirotetramat (100 OD) at a total rate of 167 g a.i./ha (0.15 lbs a.i./A, 0.9X)). The two applications were made at a 14-day RTI. Treated lettuce was harvested at maturity 7 days after the last treatment.

Greater than 95% of the TRR in lettuce was extracted with ACN/water. The TRR was 3.13 ppm, calculated by summing extracts and post extraction solids. Over 91% of the extracted radioactivity was identified. Unchanged parent compound spirotetramat was the major residue identified (55.9% of the TRR; 1.75 ppm), followed by BYI 08330-enol (17.8% of the TRR; 0.56 ppm), BYI 08330-enol-Glc (11.4% of the TRR; 0.36 ppm), and BYI 08330-ketohydroxy (6.2% of the TRR; 0.2 ppm).

The metabolism of spirotetramat in lettuce involved:

- Hydrolytic cleavage of the carbonate ester bond of the parent compound to form BYI 08330-enol and subsequent conjugation to BYI 08330-enol-Glc.
- Hydroxylation in the tetramic acid moiety resulted in BYI 08330-ketohydroxy.

Table 6. Summary of Characterization and Identification of Radioactive Residues in Lettuce Matrices Following Application of Radiolabeled Spirotetramat at 0.15 lb a.i./A/Season (0.9X).

Compound	Lettuce Heads TRR =3.13 ppm	
	% TRR	ppm
Spirotetramat	55.9	1.75
BYI 08330-ketohydroxy	6.2	0.20
BYI 08330-enol	17.8	0.56
BYI 08330-enol-Glc	11.4	0.36
Total identified	91.4	2.87
Total characterized	7.3	0.22
Total extractable	98.7	3.09
Unextractable[1]	1.3	0.04

[1] Residues remaining after exhaustive extractions.

Cotton

The metabolism of spirotetramat was investigated in cotton (gin trash, lint & undelinted seeds) following two spray applications of [azaspirodecenyl-3-^{14}C]-spirotetramat, formulated as a SC, at a total rate of 264 g a.i./ha/season (0.23 lbs. a.i./A)). The first application was made at an early growth stage (BBCH 15) at a rate of 91.7 g a.i./ha, and the second at growth stage 85 (134 days interval) at a rate of 172.3 g a.i./ha. One immature cotton plant sample was collected at 19 days after the first application. Cotton gin trash, lint and undelinted seed samples were harvested 39 days after the last treatment.

The TRR was 2.381 ppm in the immature plant sample, 1.641 ppm in gin trash, 1.078 ppm in lint, and 0.119 ppm in undelinted seed.

Parent compound, spirotetramat, was the major residue (46.95% of the TRR, 1.117 ppm) identified in the immature cotton plant. Also identified were 13 minor metabolites ranging from

0.18% to 9.76% of the TRR (0.004-0.232 ppm).

The major residues identified in cotton gin trash were BYI 08330-ketohydroxy (29.7% of the TRR; 0.478 ppm), spirotetramat (19.8% of the TRR; 0.319 ppm), and BYI 08330-enol (12.1% of the TRR; 0.196 ppm). The major residues identified in cotton lint were spirotetramat (32.3% of the TRR; 0.348 ppm), BYI 08330-mandelic acid amide (11.9% of the TRR; 0.128 ppm), and BYI 08330-ketohydroxy (10.5% of the TRR; 0.113 ppm). The major residue found in the cotton undelinted seeds was BYI 08330-enol (39.8% of the TRR; 0.047 ppm), while BYI 08330-ketohydroxy represented 9.04% of the TRR (0.011 ppm). Ten metabolites representing 0.6-4.4% of the TRR (0.003-0.064 ppm) were also identified in the gin trash, lint and undelinted seeds.

The major metabolic step for spirotetramat in cotton involved the hydrolysis of the ethyl carbonate group to form BYI 08330-enol (figure 1). Oxidation of the pyrroline moiety of BYI 08330-enol led to the formation of BYI 08330-ketohydroxy. Cleavage of the pyrroline ring of BYI 08330-ketohydroxy followed by decarboxylation and hydrolysis yielded BYI 08330-MA-amide, BYI 08330-olefin, BYI 08330-mandelic acid amide, and BYI 08330-mandelic acid. Demethylation of the cyclohexyl methoxy group of BYI 08330-enol and BYI 08330-ketohydroxy and conjugation led to the formation of BYI 08330-desmethyl-ketohydroxy and the glucoside and BYI 08330-desmethyl-enol-Glc. Other minor metabolic reactions involved ring closure of BYI 08330-MA-amide to form a morpholine ring and conjugation of BYI 08330-enol with glucose.

Table 7. Summary of Characterization and Identification of Radioactive Residues in Cotton Matrices Following Application of Radiolabeled Spirotetramat at 0.23 lb a.i./A.

Metabolite Fraction	Intermediate		Gin Trash		Lint		Undelinted Seed	
	TRR=2.381 ppm		**TRR=1.614 ppm**		**TRR=1.078 ppm**		**TRR=0.119 ppm**	
	%TRR	ppm	%TRR	ppm	%TRR	ppm	%TRR	ppm
-enol-Glc	4.65	0.111	-	-	-	-	-	-
-mandelic acid	-	-	-	-	0.89	0.010	-	-
-mandelic acid amide	0.36	0.009	1.65	0.027	11.87	0.128	1.30	0.002
-desmethyl-enol-Glc	3.82	0.091	1.75	0.028	-	-	3.46	0.004
-desmethyl-ketohydroxy-Glc (I1)	3.45	0.082	1.42	0.023	0.14	0.001	-	-
-desmethyl-ketohydroxy-Glc (I2)	6.31	0.150	2.32	0.038	-	-	-	-
-hydroxymorpholinedion	0.61	0.014	0.64	0.01	-	-	-	-
-desmethyl-ketohydroxy	0.18	0.004	0.56	0.009	-	-	-	-
-MA-amide	0.58	0.014	1.54	0.025	4.12	0.044	-	-
-enol	1.98	0.047	12.09	0.196	9.46	0.101	**39.81**	**0.047**
-ketohydroxy	5.40	0.129	**29.65**	**0.478**	10.45	0.113	9.04	0.011
BYI 08330-olefine(I1)	0.54	0.013	1.76	0.028	4.08	0.044	-	-
BYI 08330-olefine(I2)	0.43	0.010	2.04	0.033	4.35	0.047	-	-
Spirotetramat (a.i.)	**46.94**	**1.117**	19.78	0.319	**32.32**	**0.348**	0.42	<0.001
Total Identified (conventional extraction methods)	75.3	1.791	79.2	1.278	77.7	0.837	22.9	0.027
Total Identified after exhaustive extraction methods	-	-	-	-	-	-	34.6	0.041
Total Identified Overall	75.3	1.791	79.2	1.278	77.7	0.837	57.5	0.068
Total Characterized	8.8	0.210	9.4	0.152	14.8	0.160	13.9	0.017
Total Extractable	84.1	2.002	88.6	1.430	92.5	0.997	80.5	0.096
Total Bound	15.9	0.379	11.4	0.184	7.5	0.080	9.6	0.011

Potato

The metabolism of spirotetramat was investigated in potatoes (tuber & tops) following three spray applications of [azaspirodecenyl-3-^{14}C]-spirotetramat, formulated as an OD, at a total rate

of 308 g a.i./ha (0.275 lbs. a.i./A, 1.7X). The applications were made at a 21-day RTI. Potato samples were harvested 14 days after the last treatment.

Approximately 80% of the TRR in tuber, and 96% of the TRR in tops were extracted with ACN/water. Enzymatic treatment of the extracted tuber released approximately 14% of the TRR. The TRR in tuber and tops was 0.255 ppm and 11.057 ppm, respectively, calculated by summing extracts and post extraction solids.

Parent spirotetramat was not identified in potato tuber. The predominant metabolite identified was BYI 08330-enol (65.8% of the TRR; 0.168 ppm), followed by BYI 08330-ketohydroxy (6.8% of the TRR; 0.018 ppm) and BYI 08330-desmethyl-enol (6.7% of the TRR; 0.018 ppm) and several other minor metabolites (≤2.5 % of the TRR; 0.006 ppm).

In potato tops, spirotetramat and BYI 08330-ketohydroxy were the major residues identified, represented 49.4% (5.5 ppm) and 24.8% of the TRR (2.7 ppm), respectively. BYI 08330-enol (7.8% of the TRR; 0.87 ppm) and several other minor metabolites (≤3.6% of the TRR) were also identified.

The metabolism of spirotetramat in potatoes mainly involved:

- Hydrolysis of parent compound to BYI 08330-enol
- Oxidation of BYI 08330-enol to BYI 08330-ketohydroxy
- Conjugation of BYI 08330-enol to BYI 08330-enol-Glc
- *O*-Demethylation of BYI 08330-enol to BYI 08330 desmethyl-enol

Table 8. Summary of Characterization and Identification of Radioactive Residues in Potato Matrices Following Application of Radiolabeled Spirotetramat at 0.275 lb a.i./A (1.7X).

Compound	Tubers		Tops	
	TRR = 0.255 ppm		TRR = 11.057 ppm	
	% TRR	ppm	% TRR	ppm
Spirotetramat	ND	ND	49.4	5.455
BYI 08330-enol	65.8	0.168	7.8	0.870
BYI 08330-enol-Glc	2.5	0.006	3.6	0.395
BYI 08330-desmethyl-enol	6.7	0.018	1.1	0.119
BYI 08330-desmethyl-enol-glycoside	1.5	0.004	0.5	0.055
BYI 08330-enol-alcohol	0.6	0.002	0.2	0.020
BYI 08330-ketohydroxy	6.8	0.018	24.8	2.745
BYI 08330-ketohydroxy-alcohol	0.5	0.001	ND	ND
BYI 08330-ketohydroxy-alcohol-glycoside	0.5	0.001	ND	ND
BYI 08330-dihydroxy	0.2	0.001	ND	ND
Total identified	85.1	0.217	87.4	9.659
Total characterized	9.4	0.024	8.7	0.957
Total extractable	94.5	0.241	96.0	10.616
Unextractable[1]	5.5	0.014	4.0	0.442

1 Residues remaining after exhaustive extractions.

ND Not detected

Conclusions: The submitted metabolism data for apple, lettuce, cotton and potato are adequate to elucidate the nature of the residue in plants. Major metabolic reaction involved the hydrolytic cleavage of the carbonate ester parent bond of the parent compound to form BYI 08330-enol.

Further reduction of the double bond in the teramic acid moiety of BYI 08330-enol occurred to form the BYI 08330-mono-hydroxy metabolite. Hydroxylation in the tetramic acid moiety resulted in BYI 08330-ketohydroxy. Demethylation of the methoxy group of the cyclohexyl ring resulted via a proposed intermediate (BYI 08330-desmethyl-enol) in BYI 08330-desmethyl-ketohydroxy (after the corresponding hydroxylation). Oxidation of the methoxy group resulted in BYI 08330-ketohydroxy-formiate. Partly, metabolites bearing a hydroxy group were conjugated with glucose. The residues of concern for the tolerance expression and risk assessment for plant commodities are spirotetramat and its metabolites BYI 08330-enol, BYI 08330-ketohydroxy, BYI08330-enol-Glc, and BYI 08330-mono-hydroxy (Memo, J. Tyler *et al.*, 4/16/08; D333437).

FIGURE 1. Proposed Metabolic Profile of Spirotetramat in Cotton.

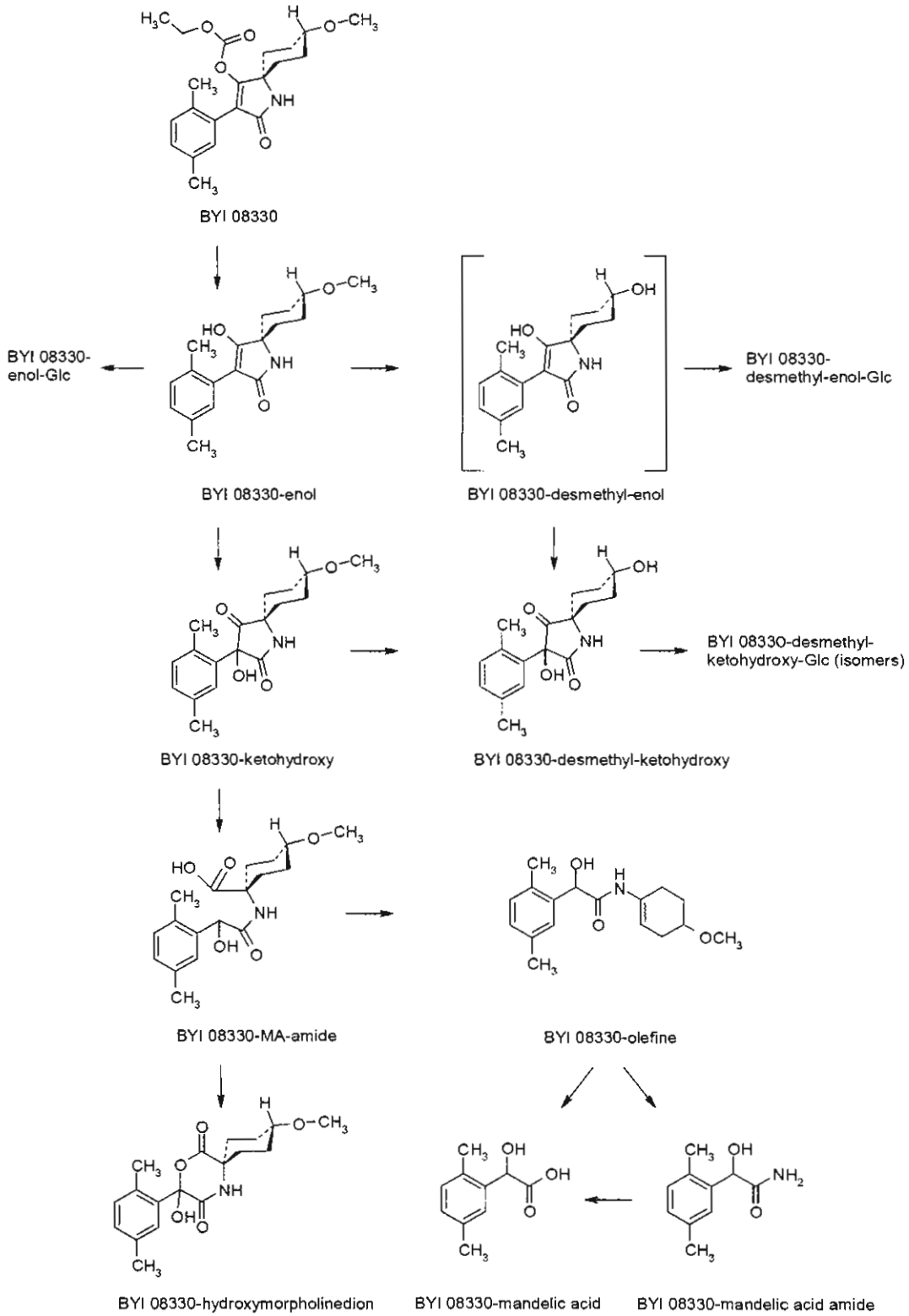
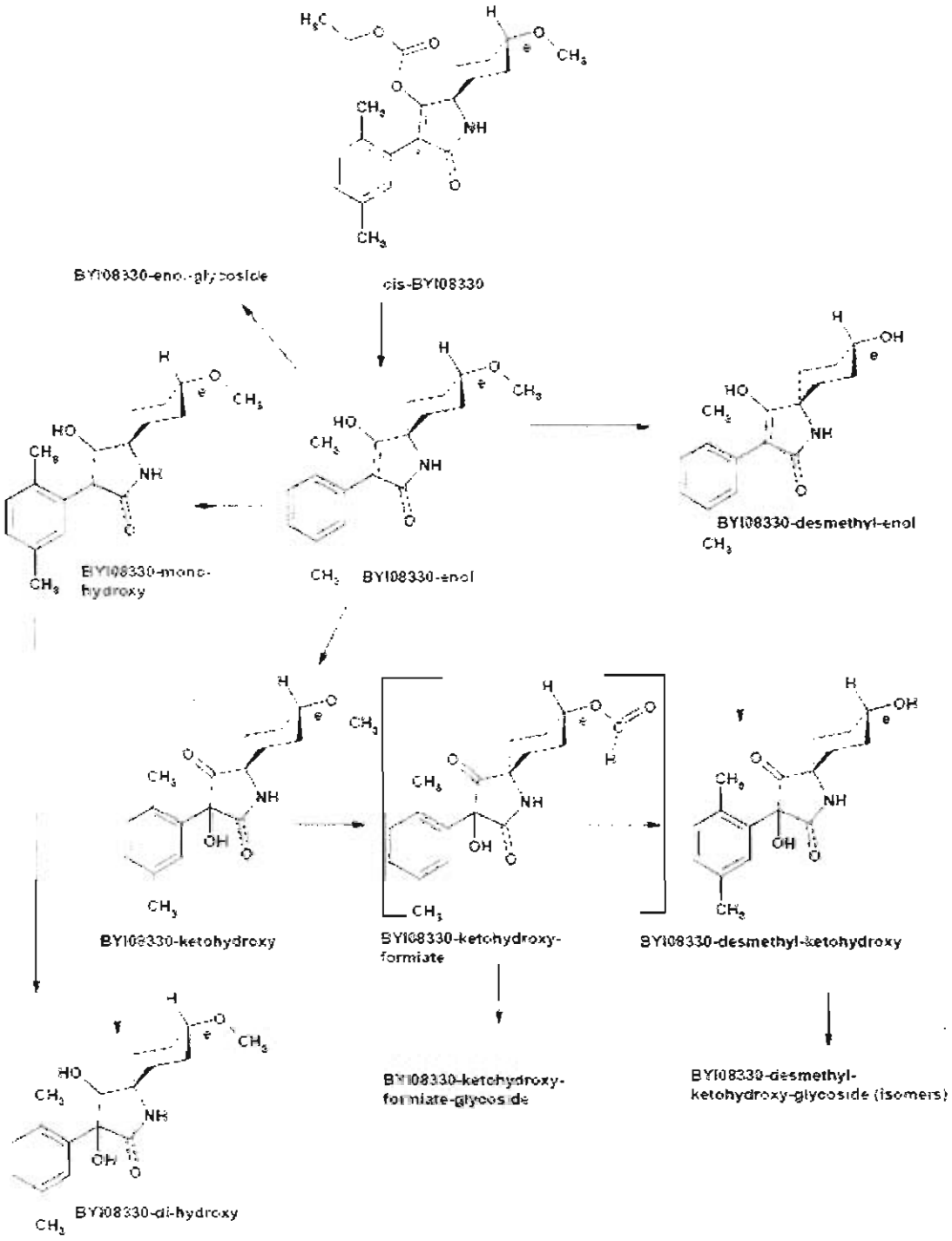


FIGURE 2. Proposed Metabolic Profile of Spirotetramat in Apple Fruit and Leaves.



860.1300 Nature of the Residue - Livestock

DER Reference List 46904482.der.doc (Goat)
46904483.der.doc (Hen)

Goat

The nature of the residue in ruminant tissues and milk was investigated with a lactating goat following 4 daily oral administrations of [azaspirodecenyl-3-^{14}C]-spirotetramat at a mean dose rate of 2.22 mg a.i./kg bw/day (73.03 ppm in feed, 61X) given by gavage. Milk samples were collected twice daily, urine and feces were collected once daily. The treated goat was sacrificed ~24 hrs after the last dosage, and muscle (round, flank, loin), fat (perirenal, omental subcutaneous), liver, and kidneys were collected.

Approximately 90% of the administrated dose (AD) was eliminated via urine (78.4%), feces (11.6%), milk (0.014%), and edible organs/tissues (0.061%). The highest TRR was observed in kidney (0.184 ppm) and liver (0.05 ppm). Significantly lower residues were detected in the muscle: round muscle (0.011 ppm), flank muscle (0.009 ppm), and loin muscle (0.008 ppm); and fat: subcutaneous fat (0.008 ppm), omental fat (0.003 ppm), and perirenal fat (0.003 ppm). The TRR in milk samples was in the range of 0.0038-0.0261 ppm within the observation period of 96 hours.

The parent compound was not detected in samples of milk, muscle, fat, liver and kidney. The major metabolites detected were BYI 08330-enol (33.7-78.4% of the TRR) and BYI 08330-enol-glucuronide (14.2-37.4% of the TRR). Three other minor metabolites (BYI 08330-ketohydroxy, BYI 08330-desmethyl-enol, and BYI 08330-mono-hydroxy) were found each at less than 10% of the TRR.

The metabolism of spirotetramat in ruminants involved cleavage of the carbonate ester group to the primary metabolite BYI 08330-enol followed by conjugation of the enol hydroxy group with glucuronic acid to BYI 08330-enol-GA. Oxidation of the azaspirodecenyl moiety to BYI 08330-ketohydroxy and demethylation of the methoxy group to BYI 08330-desmethyl-enol were minor metabolic reactions as well as reduction of the azaspirodecenyl moiety to BYI 08330-monohydroxy.

Table 9. Summary of Characterization and Identification of Radioactive Residues in Goat Matrices Following Application of ^{14}C-Spirotetramat at 73.03 ppm (61X) in Feed for 4 Consecutive Days.

Compound	Muscle		Fat		Liver		Kidney		Milk (day 4)	
	TRR = 0.011 ppm		TRR = 0.003 ppm		TRR = 0.050 ppm		TRR = 0.184 ppm		TRR = 0.008 ppm	
	% TRR	ppm	% TRR	ppm	% TRR	ppm	% TRR	ppm	%TRR	ppm
Parent Spirotetramat	--	--	--	--	--	--	--	--	--	--
BYI 08330-enol-GA	--	--	**19.4**	0.001	**37.4**	0.019	**14.2**	0.026	**23.9**	0.002
BYI 08330-desmethyl-enol	7.4	0.001	--	--	6.6	0.003	4.4	0.008	7.9	0.001
BYI 08330-mono-hydroxy	--	--	--	--	4.1	0.002	--	--	2.3	<0.001
BYI 08330-enol	**72.4**	0.008	**59.9**	0.002	**33.7**	0.017	**78.4**	0.144	**48.8**	0.004
BYI 08330-ketohydroxy	9.7	0.001	--	--	2.7	0.001	2.1	0.004	2.3	<0.001
Unknown	--	--	--	--	10.7	0.005	0.9	0.002	14.9	0.001

Table 9. Summary of Characterization and Identification of Radioactive Residues in Goat Matrices Following Application of ^{14}C-Spirotetramat at 73.03 ppm (61X) in Feed for 4 Consecutive Days.

Compound	Muscle		Fat		Liver		Kidney		Milk (day 4)	
	TRR = 0.011 ppm		TRR = 0.003 ppm		TRR = 0.050 ppm		TRR = 0.184 ppm		TRR = 0.008 ppm	
	% TRR	ppm	% TRR	ppm	% TRR	ppm	% TRR	ppm	%TRR	ppm
Total identified	89.6	0.010	79.3	0.002	84.3	0.042	99.1	0.182	85.1	0.007
Total characterized	--	--	--	--	10.7	0.005	0.9	0.002	14.9	0.001
Total extractable	89.6	0.10	79.3	0.002	95.0	0.047	100	0.184	100	0.008
Unextractable[1]	--	--	20.7	0.001	4.7	0.002	--	--	--	--

[1] Residues remaining after extractions.

Hen

The nature of the residue in eggs and tissues was investigated with 6 laying hens dosed orally once daily by gavage with [azaspirodecenyl-3-^{14}C]spirotetramat at a rate of 1.01 mg a.i./kg bw/day (12.86 ppm in feed) for 14 days. Eggs and excreta were collected daily. The treated hens were sacrificed ca. 24 hrs after the last dosage. Liver, kidney, muscle (leg, breast), fat (subcutaneous), skin (without fat) were collected.

The majority of the radioactivity (90% of the AD) was detected in the excreta. Only 0.045% and 0.023% of the total AD were detected in the eggs and edible organs/tissues, respectively. The highest TRR was detected in kidneys (0.039 ppm) and liver (0.017 ppm), followed by fat (0.004 ppm), and muscle (0.003 ppm). The average TRR in eggs was 0.015 ppm.

The parent compound was not detected in any of the samples. BYI 08330-enol was the major metabolite detected in eggs, liver, fat and muscle (18-84% of the TRR; 0.001-0.013 ppm). The glucuronic acid conjugate BYI 08330-enol-GA was also detected in eggs (6.9% of the TRR, 0.001 ppm), muscle (4.2% of the TRR, <0.001 ppm) and liver (15.1% of the TRR, 0.003 ppm).

The metabolism of spirotetramat in the laying hen appeared to be via cleavage of the carbonate ester bond of the side chain to BYI 08330-enol followed by conjugation with glucuronic acid.

Table 10. Summary of Characterization and Identification of Radioactive Residues in Hen Matrices Following Application of ^{14}C-Spirotetramat at 1.01ppm bw for 14 Consecutive Days.

Compound	Muscle		Fat		Liver		Eggs	
	TRRs = 0.003 ppm		TRRs = 0.004 ppm		TRRs = 0.017 ppm		TRRs = 0.015 ppm	
	% TRR	ppm	% TRR	ppm	% TRR	ppm	%TRR	ppm
Spirotetramat	--	--	--	--	--	--	--	--
BYI 08330-enol-GA	4.2	<0.001	--	--	15.1	0.003	6.9	0.001
Unknown 1	6.9	<0.001	--	--	3.6	0.001	4.7	0.001
BYI 08330-enol	64.4	0.002	18.4	0.001	50.0	0.009	83.9	0.013
Unknown 2[1]	--	--	56.5	0.002	--	--	--	--
Total identified	68.6	0.002	18.4	0.001	65.1	0.011	90.8	0.014
Total characterized	6.9	<0.001	56.5	0.002	3.6	0.001	4.7	0.001
Total extractable	75.6	0.002	74.9	0.003	68.6	0.012	95.5	0.014
Unextractable[2]	24.4	0.001	25.1	0.001	30.0	0.005	4.5	0.001

[1] Presumably fatty acid conjugate of BYI 08330-enol or related metabolite.

[2] Residues remaining after exhaustive extractions.

Conclusions: The submitted goat and poultry metabolism data are adequate to satisfy data

requirements. The biodegradation of spirotetramat in livestock can be characterized as cleavage of the carbonate ester group to the primary metabolite BYI 08330-enol followed by conjugation of the enol hydroxy group with glucuronic acid to BYI 08330-enol-GA. Oxidation of the azaspirodecenyl moiety to BYI 08330-ketohydroxy and demethylation of the methoxy group to BYI 08330-desmethyl-enol were minor metabolic reactions in ruminants as well as reduction of the azaspirodecenyl moiety to BYI 08330-monohydroxy. Based on the currently proposed uses, the residues of concern for the tolerance expression for livestock commodities are spirotetramat and its metabolite BYI 08330-enol and the residues of concern for the risk assessment for livestock commodities are spirotetramat and its metabolites BYI 08330-enol and BYI 08330-enol-GA (Memo, J. Tyler *et al.*, 4/16/08; D333437). If future proposed uses result in significant exposure of livestock to the plant metabolites BYI 08330-ketohydroxy, BYI08330-enol-Glc, and BYI 08330-mono-hydroxy, then these metabolites may need to be included as additional residues of concern for livestock commodities.

860.1340 Residue Analytical Methods

Plant methods

DER Reference List 47151105.der.doc (Includes MRIDs 46904487, 46904489, 46904485, 46904494, 46904506, 47151103, and 47151104); HPLC-MS/MS Method, 00857, 00888, and 00929

HPLC-MS/MS Analytical Method 00857

Analytical method 00857 was developed for the determination of residues of spirotetramat, the metabolites BYI 08330-enol, BYI 08330-ketohydroxy, BYI 08330-mono-hydroxy and BYI 08330-enol-Glc in plant matrices by HPLC-MS/MS using isotopically labeled internal standards. Spirotetramat, BYI 08330-enol, BYI 08330-ketohydroxy, BYI 08330-mono-hydroxy and BYI 08330-enol-Glc were extracted from the plant commodity using a blender with acidic ACN/water (4/1, v/v). After subsequent clean-up of the extract through a BondElut clean polyethylene frit, the corresponding internal standards were added. The solution was made up to volume, diluted and subjected to HPLC-MS/MS with multiple-reaction monitoring of two transitions for each matrix and analyte for quantitation and confirmation purposes. The limit of quantitation (LOQ) was 0.01 ppm for each analyte on all tested plant commodities with the exception of hop cones (0.1 ppm). The limit of detection (LOD) for all analytes was estimated to be at about 4 times lower than the corresponding LOQ. The detector response was linear over the range of 5 ng/L to 50 µg/L (r^2>0.997).

Method 00857 was adequately validated on orange (fruit, juice, pomace, & jam), cherry (sweet & sour), plum, peach, strawberry, apple (fruit, dried pomace, & sauce), tomato (fruit, juice, & preserve), grape (fruit, must, pomace, & wine), potato, melon (peel & pulp), onion bulb, hop (beer, dried & green cones), broccoli, cauliflower, lettuce head, pepper, cucumber, mandarin (fruit & peel), cabbage, Chinese kale, kohlrabi (tuber & leaf), Brussels sprout, French climbing bean (bean with pod), apricot, pear, almond nutmeat, wheat (straw, forage, grain, & flour), peanut (nutmeat & oil), sugar beet (root & molasses), Swiss chard, and cotton seed. Mean recoveries of all analytes from all tested matrices were within the acceptable range of 70-120% with a relative standard deviation (RSD) <16%.
Analytical method 00929 was developed for the determination of the residues of BYI 08330-

ketohydroxy-alcohol, BYI 08330-desmethyl-ketohydroxy, and BYI 08330-desmethyl-di-hydroxy in rotational crops. The residues in plants were extracted with ACN/water (1/1, v/v) using a blender, and an acid hydrolysis step was incorporated to release the conjugate metabolites. After filtration, the extract was cleaned on a polystyrenedivenylbenzene column and the corresponding internal standards were added. The solution was made up to volume and subjected to HPLC-MS/MS. Two HPLC columns were used for quantitation and confirmation purposes. The LOQ was 0.02 ppm for each analyte. The method/detector response was linear (coefficient of determination, $r^2 \geq 0.997$) within the range of 0.02-20 µg/L. Method 00929 was validated on untreated samples of wheat (grain, forage, straw and flour), cotton undelinted seeds, Swiss chard, peanut (oil and nutmeat), and sugar beets (roots and molasses) spiked with each analyte at 0.02 ppm and 0.20 ppm. Mean recoveries of all analytes from all matrices were within the acceptable range of 70-120% with RSD <11%.

An enforcement method (method 00888) was developed to determine residues of spirotetramat and the metabolite BYI 08330-enol in/on plant matrices by HPLC-MS/MS. Spirotetramat and BYI 08330-enol were extracted from citrus fruit, tomato, potato, avocado and dried hop cones with acidic ACN/water (4/1, v/v) using a blender. After subsequent clean-up through Strata C18-E tube, the extract was made up to volume, diluted and subjected to HPLC-MS/MS with monitoring of two multiple-reaction monitoring transitions. Residues were quantified against external matrix matched standards. The recoveries from samples of citrus fruit, tomato, potato and avocado spiked with each analyte at 0.01 and 0.1 ppm, and from samples of dried hop cones spiked at 0.1 and 1.0 ppm were within the acceptable range of 70-120% with RSD <18%.

Both analytical methods 00857 and 00888 had been successfully validated by independent laboratories. The extraction efficiencies of methods 00857 and 00929 were tested using incurred samples from the metabolism studies. The recoveries of the extracted radioactive residues of spirotetramat and the metabolites were in agreement with those generated in the metabolism studies.

Livestock methods

DER Reference List	46904492.der.doc (Includes MRIDs 46904495, 46904490, 47151101, 47151102, and 46904491); HPLC-MS/MS Method 00966

HPLC-MS/MS Method No. 00966

The analytical method 00966 was developed for the determination of residues of spirotetramat and the metabolites BYI 08330-enol and BYI 08330-enol-GA in livestock matrices by high-performance HPLC-MS/MS using isotopically labeled internal standards. Spirotetramat, BYI 08330-enol and BYI 08330-enol-GA were extracted from the sample material (fat, liver, kidney) using a blender with an acidic ACN/water mixture (7/3, v/v). Milk and muscle were extracted using a blender with acidic ACN and subsequent clean-up of the extract through a Varian MEGA BE-C18 cartridge. The corresponding isotopically labeled internal standards were added. The solution was made up to volume, diluted and subjected to HPLC-MS/MS with multiple-reaction monitoring. Two multiple-reaction monitoring transitions were monitored for each matrix and each analyte for quantitation and confirmation purposes.

The validated LOQ was 0.01 ppm in tissues, and 0.005 ppm in milk for each analyte. The LOD

for all analytes was estimated to be about 10 times lower than the corresponding LOQ. The detector response was linear over the range of 0.02-20 µg/L (r^2 >0.999).

The data-gathering method was validated for each analyte at concentration levels of 0.01 and 0.10 ppm in cattle and poultry muscle, cattle fat, cattle liver and cattle kidney; and 0.005 and 0.050 ppm in milk. Minor modifications were applied to the cleanup step for some matrices. The percent recoveries from all matrices were 68-101% (spirotetramat), 75-101% (BYI 08330-enol), and 69-105% (BYI 08330-enol-GA). Mean recoveries of all analytes from all matrices were within the acceptable range of 70-120% with RSD ≤9%.

An enforcement method (method 00969) was developed to determine residues of BYI 08330-enol in/on matrices of livestock origin (muscle, kidney, egg and milk) by HPLC-MS/MS. BYI 08330-enol was extracted from egg and kidney using a blender with an ACN/water mixture (7/3, v/v). Milk and muscle were extracted using a blender with ACN. After subsequent clean-up of the extract through a C18 cartridge, the solution was made up to volume, diluted and subjected to HPLC-MS/MS. For calibration, matrix-matched standards were used (i.e., standards were prepared in extracts from untreated samples). Same as method 00966, two multiple-reaction monitoring transitions were monitored for BYI 08330-enol in each matrix, *m/z* 302-216 (quantitation) and *m/z* 302-270 (confirmation). The recoveries from samples of cattle muscle, cattle kidney, and egg spiked at 0.01 and 0.10 ppm; and milk spiked at 0.005 and 0.050 ppm were within the acceptable range of 91-99% with RSD ≤6%.

An independent laboratory validation (ILV) of method 00969 using milk, cattle meat, and egg was successful and supports the method's LOQ of 0.01 ppm for BYI 08330-enol in meat and egg, and 0.005 ppm in milk. An extraction efficiency study was not considered necessary since method 00966 uses the same extraction solvents as those used in the livestock metabolism study.

Conclusions: The petitioner has submitted several HPLC-MS/MS residue analytical methods for the determination of residues of the parent and its metabolites in/on plant and livestock commodities. Analytical method 00857 was developed for the determination of residues of spirotetramat, the metabolites BYI 08330-enol, BYI 08330-ketohydroxy, BYI 08330-monohydroxy and BYI 08330-enol-Glc in plant matrices by HPLC-MS/MS. The analytical method 00966 was developed for the determination of residues of spirotetramat and the metabolites BYI 08330-enol and BYI 08330-enol-GA in livestock matrices by HPLC-MS/MS. These methods were used as the data-collection methods in the analysis of samples for residues of concern from the various studies associated with the current petition. Each method has been adequately validated by the petitioner as well as by independent laboratories. Methods 00857 and 00966 were also adequately radiovalidated using weathered samples obtained from metabolism studies.

HED has determined that Methods 00857 and 00966 are suitable enforcement methods for plant and livestock commodities, respectively, since the methods passed a successful PMV by Agency chemists at ACL/BEAD (E-mail, C. Stafford to D. Vogel; 2/19/08).

860.1360 Multiresidue Methods (MRM)

DER Reference List 46904496.der.doc

Spirotetramat and five metabolites BYI 08330-enol, BYI 08330-ketohydroxy, BYI 08330-mono-hydroxy, BYI 08330-enol-Glc, and BYI 08330-enol-GA were screened through multiresidue methods described in the U.S. Food and Drug Administration (FDA) Pesticide Analytical Manual, Vol. I (PAM I). Spirotetramat and the metabolites were tested for natural fluorescence using procedures outlined in Protocol A of PAM I. BYI 08330-mono-hydroxy was the only compound found to be naturally fluorescent; no further test with this protocol was performed.

Spirotetramat and its metabolites were subjected to Protocol C, modules DG1, DG5, DG13, DG17 and DG18. Due to the poor sensitivity of the test substances to detection by method described in Protocol C, no further analyses were performed for Protocols D, E, or F. Since the test substances are not acidic, phenols or substituted ureas, analyses were not performed using Protocols B or G.

Conclusions. The MRMs are not suitable for the analysis of spirotetramat or its metabolites. The multiresidue methods testing data will be forwarded to FDA for further evaluation and inclusion of results in PAM Vol. I.

860.1380 Storage Stability

Plant commodities

DER Reference List 47244601.der.doc (Primary Crops)
46904497.der.doc (Rotational Crops)

Primary Crops

Samples of tomato (fruit and paste), potato (tuber), lettuce (head), climbing French bean (bean with pod) and almond (nutmeat) were spiked separately with 0.2 ppm of each spirotetramat, BYI 08330-enol, BYI 08330-ketohydroxy, BYI 08330-mono-hydroxy, BYI 08330-enol-Glc and stored at -18°C for approximately 30, 60, 90, 180, 370, 540, and 718 days. Samples were analyzed by HPLC-MS/MS method 00857. Adequate method validation data were provided.

Samples spiked with spirotetramat were analyzed for all analytes and the total residues were expressed as spirotetramat equivalents. Samples spiked with BYI08330-enol were also analyzed for all analytes, with the exception of spirotetramat, and the total residues were expressed as BYI08330-enol equivalents. Samples that were spiked with BYI08330-ketohydroxy or BYI08330-mono-hydroxy or BYI08330-enol-Glc were analyzed and reported individually.

Total spirotetramat residues were stable (<30% degradation) in all matrices during freezer storage for up to 718 days. Total BYI08330-enol residues declined by 35% in tomato paste after 715 days of freezer storage. Residues of BYI 08330-ketohydroxy, -mono-hydroxy and -enol-Glc were stable (<30% degradation) in all matrices analyzed for up to 718 days.

A second study was performed to examine the effects of frozen storage on spirotetramat residues in orange juice and prunes. Samples of orange juice and prune fruit were spiked individually with 0.20 ppm of each spirotetramat, BYI 08330-enol, BYI 08330-ketohydroxy, BYI 08330-monohydroxy, BYI 08330-enol-Glc and stored at <-18°C. Spiked samples were analyzed using method 00857 (LC-MS/MS method) at 0-, 30-, 90-, and 144/147-day intervals. Total residues of spirotetramat in orange juice and prunes were stable (<30% degradation) during frozen storage for up to 147 days.

Rotational Crops

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

Sample storage conditions and intervals

The storage intervals and conditions of samples from the residue field trials, rotational crop field trials, and processing studies which were submitted to support this petition are presented in Table 11.

Table 11. Summary of Storage Conditions and Intervals of Samples from Crop Field Trial, Processing, and Field Rotational Crop Studies.

Matrix	Storage Temperature (°C)	Actual Storage Duration for Most Samples (days)	Interval of Demonstrated Storage Stability
***Brassica* Leafy Vegetables (MRID 46904509)**			
Broccoli	<-10	518	Total residues are stable in tomato fruit, potato tubers, lettuce heads, climbing French bean, and almond nutmeat during frozen storage for up to 715 days and in orange juice for at least 150 days.
Cauliflower	<-10	600	
Mustard Greens	<-10	731	
Citrus (MRIDs 46904514 & 46904522)			
Orange	<-10	412	See above for *Brassica* Leafy Vegetables.
Lemon	<-10	362	
Grapefruit	<-10	245	
Citrus Processed Commodities	<-15	12-169	
Cucurbit Vegetables (MRID 46904511)			
Cucumber	<-15	707	See above for *Brassica* Leafy Vegetables.
Muskmelon	<-15	686	
Summer Squash	<-15	708	
Fruiting Vegetables (MRID 46904510 & 46904512)			
Tomato	<-15	677	See above for *Brassica* Leafy Vegetables.

Table 11. Summary of Storage Conditions and Intervals of Samples from Crop Field Trial, Processing, and Field Rotational Crop Studies.

Matrix	Storage Temperature (°C)	Actual Storage Duration for Most Samples (days)	Interval of Demonstrated Storage Stability
Bell Pepper	<-15	678	
Non-Bell Pepper	<-15	649	
Tomato Processed Commodities	<-15	642-658	
Grapes (MRID 46904517 & 46904521)			
Grapes	<-15	281	See above for *Brassica* Leafy Vegetables.
Grape Processed Commodities	<-10	128-171	
Hops (MRID 46904518)			
Hop Cones	<-10	321	See above for *Brassica* Leafy Vegetables.
Leafy Vegetables (MRID 46904508)			
Head Lettuce	<-10	507	See above for *Brassica* Leafy Vegetables.
Leaf Lettuce	<-10	449	
Celery	<-10	**650**	
Spinach	<-10	448	
Pome Fruit (MRIDs 46904515 & 46904520)			
Apple Fruit	-27.4 to -9.1	140	See above for *Brassica* Leafy Vegetables.
Pear Fruit	-28.3 to 0.8	175	
Apple Processed Commodities	<-15	34-90	
Potato (MRID 46904519 & 46904524)			
Potato tubers	<-10	382	See above for *Brassica* Leafy Vegetables.
Potato Processed Commodities	<-15	8-11	
Stone Fruit (MRID 46904513 & 46904523)			
Cherry	<-10	390	See above for *Brassica* Leafy Vegetables.
Peach	<-10	364	
Plum	<-10	333	
Prune	<-10	140	
Tree Nuts (MRID 46904516)			
Almond Nutmeat	<-10	339	See above for *Brassica* Leafy Vegetables.
Almond Hulls	<-10	330	
Pecan Nutmeat	<-10	256	
Rotational Crop Study: Mustard Greens, Turnips, and Wheat as the Rotational Crops (MRID 46904526)			
Mustard greens	<-15	≤464	BYI 08330-ketohydroxy, BYI 08330-desmethyl-di-hydroxy, BYI 08330-desmethyl-ketohydroxy and BYI 08330-ketohydroxy-alcohol are stable for 924-974 days. Spirotetramat tends to degrade with the increase of storage period.
Turnip (tops & roots)	<-15	≤462	
Wheat (forage, hay, straw & grain)	<-15	≤339	

Livestock commodities

No storage stability data were submitted for livestock commodities, and none are required to support the submitted cattle feeding study (MRID 46904501) because sample integrity was maintained by appropriate freezer storage, and all samples were analyzed within 30 days of collection.

Conclusions. Adequate storage stability data have been submitted. Total spirotetramat residues were stable (<30% degradation) in all matrices during freezer storage for up to 718 days. These data support the storage conditions and intervals of samples collected from the various crop field trials as well as the rotational crop studies. There are no unresolved storage stability issues, and no corrections need to be applied to the various residue crop studies. No storage stability data are required for livestock commodities because samples from the processing and livestock feeding studies were analyzed within 30 days of collection.

860.1480 Meat, Milk, Poultry, and Eggs

Livestock dietary burdens

The potential for secondary transfer of spirotetramat residues of concern in meat, milk, and eggs exists because there are livestock feedstuffs associated with the proposed uses on apples, citrus, potatoes, and almonds. The livestock dietary burdens of spirotetramat and its metabolites are presented in Table 12 and reflect the most recent guidance from HED (Personal Communication, J. Stokes, 11/15/07) concerning revisions of feedstuff percentages in Table 1 and constructing reasonably balanced dietary burdens (RBDBs). The calculated total dietary burdens of spirotetramat and its metabolites (based on tolerance-level residues) are 1.2 ppm for beef cattle, 1.0 ppm for dairy cattle, and 0 ppm for swine.

Table 12. Livestock Dietary Burdens for Spirotetramat and its Metabolites.

				% Diet [1]				Residue (ppm)			
Feedstuff	Type	Tolerance, ppm	% Dry Matter	Beef	Dairy	Poultry	Swine	Beef	Diary	Poultry	Swine
Almond hulls	R	9.0	90	-	10	-	-	-	1.0	-	-
Apple, wet pomace	R	0.7	40	-	10	-	-	-	(0.18)*	-	-
Citrus, dried pulp	R	0.6	88	10	10	-	-	(0.07)*	(0.07)*	-	-
Untreated forage/silage/hay/other	R	NA	-	30	20	-	-	-	-	-	-
Potato, processed waste	CC	0.6	15	30	10	-	-	1.2	(0.4)*	-	-
Untreated grain /grain milled byproducts/other)	CC	NA	-	20	30	80	80	-	-	-	-
Untreated oilseed meal/other	PC	NA	-	10	10	20	20	-	-	-	-
Totals				100	100	100	100	**1.2**	**1.0**	**0**	**0**

[1] All data are based on Table 1 Feedstuffs (October 2006), a revision of feedstuffs data found in Table 1 (180.1000 OPPTS Test Guidelines). Residue levels for beef and dairy are corrected for moisture content and are determined by formula: tolerance / %DM x % in diet. Residue levels for poultry and swine are considered "as-is" and are determined by formula: tolerance x % in diet. R: roughage; CC: carbohydrate concentrate; PC: protein concentrate.

* Values in the ()s are not considered based on following: Currently, since these feedstuffs are generated in limited supply seasonally and/or locally, but not in the same geographical areas, then only 1 of 4; i.e., the one that gives the highest dietary burden, is considered.

Livestock feeding studies

DER Reference List 46904501.der.doc (Dairy cattle feeding study)
Poultry feeding waiver request

Dairy cattle feeding study

Spirotetramat was administered via capsule to ten lactating Holstein dairy cows for 29 consecutive days. The target dose rates (based on feed dry weight) were 0 ppm feed/day (control), 3.0 ppm feed/day (2.5X), 9.0 ppm feed/day (7.5X), or 30 ppm feed/day (25X). Milk was collected twice daily during the dosing period. Milk samples from the 30-ppm dose group were analyzed for spirotetramat residue on study days 0, 1, 3, 7, 10, 14, 17, 21, 24, 26, and 28. Additionally, a portion of the 26-day milk sample from the 30-ppm dose group was separated into milk fat (cream) and skim milk, and each was analyzed. On day 29, the animals were sacrificed and liver, kidney, composite muscle, and composite fat were collected for analysis. The tissue and milk samples in this study were analyzed within 19 days of collection; therefore, freezer storage stability studies on beef tissue and milk matrices were not required.

The total spirotetramat residue in tissue and milk samples was quantitated by HPLC-MS/MS using isotopically labeled internal standards. The individual analyte residues of spirotetramat (parent) and the metabolites BYI 08330-enol, and BYI 08330-enol-GA, were summed to give a total spirotetramat residue in parent equivalents. The LOQ was 0.005 ppm for each analyte in milk matrices and was 0.010 ppm for each analyte in the tissue matrices.

Total spirotetramat residue in the milk samples from the 30-ppm feeding level were at or below the LOQ (0.005 ppm) in all cows throughout the study with the exception of a maximum residue of 0.006 ppm in one cow on study day 10. Residues of parent equivalents did not concentrate in samples of skim milk or milk fat separated from whole milk.

A low tissue burden was observed, with the highest residues found in kidney at the three dosing levels (0.022 ppm, 0.075 ppm and 0.274 ppm, respectively). Despite the variability in the amount of total spirotetramat residues, there appeared to be a linear relationship with the dosing levels in kidney, fat and liver tissues at the three feeding levels. At the 3-ppm dosing level, average residues of spirotetramat equivalents were less than the LOQ (0.01 ppm) in fat, muscle and liver. The total average spirotetramat residues were <0.010 ppm (muscle), 0.012 ppm (fat), and 0.016 ppm (liver) at the 9-ppm dosing level. At the 30-ppm dosing level, the total average spirotetramat residues in muscle, fat and liver were 0.012 ppm, 0.028 ppm, and 0.040 ppm, respectively.

TABLE 13. Summary of Residue Data from Lactating Cattle Feeding Study with Spirotetramat.

Matrix	Feeding Level (ppm)	Total Spirotetramat Residue Levels (ppm)[1]					
		n	Min.	Max.	Median	Mean	Std. Dev.
Milk	30	30	<0.005	0.006	< 0.005	<0.005	0.0006
Milk fat	30	3	<0.005	<0.005	<0.005	<0.005	-
Skim Milk	30	3	<0.005	<0.005	<0.005	<0.005	-
Fat	3	3	<0.010	<0.010	<0.010	<0.010	-
Fat	9	3	<0.010	0.017	<0.010	0.0123	0.004
Fat	30	3	<0.010	0.038	0.037	0.0283	0.016

TABLE 13. Summary of Residue Data from Lactating Cattle Feeding Study with Spirotetramat.							
Matrix	Feeding Level (ppm)	Total Spirotetramat Residue Levels (ppm)[1]					
		n	Min.	Max.	Median	Mean	Std. Dev.
Kidney	3	3	0.021	0.025	0.021	0.022	0.002
Kidney	9	3	0.051	0.103	0.070	0.075	0.026
Kidney	30	3	0.184	0.437	0.200	0.274	0.142
Muscle	3	3	<0.010	<0.010	<0.010	<0.010	-
Muscle	9	3	<0.010	<0.010	<0.010	<0.010	-
Muscle	30	3	<0.010	0.016	0.011	0.012	0.003
Liver	3	3	<0.010	<0.010	<0.010	<0.010	-
Liver	9	3	0.013	0.018	0.016	0.016	0.003
Liver	30	3	0.031	0.057	0.032	0.040	0.015

[1] The residues of all three analytes (greater than the respective analyte LOD) were summed to obtain the total spirotetramat residue for the sample. For the purpose of calculating the total spirotetramat residue, individual analyte residues that were reported as less than the LOQ were assigned a finite value of the LOQ.

Expected secondary residues in meat and milk

To determine the need for tolerances for spirotetramat residues of concern in milk and tissues, the anticipated secondary residues in cattle matrices were estimated using transfer coefficient factors calculated from the maximum residues of spirotetramat and its metabolites observed at the 30-ppm dose level. The transfer coefficients (calculated as residue-level-to-feed ratios) are presented in Table 14. The transfer coefficient for each matrix was then used to calculate the expected secondary residues by multiplying the transfer coefficient by the calculated dietary burden (Table 13).

Table 14. Residue-Level-to-Feed Ratios (Transfer Coefficients) in Dairy Cattle Milk and Tissues[1].			
Matrix	Maximum Residue (ppm)	Feeding Level, ppm	Transfer Coefficient
Milk	0.011	30	0.00037
Fat	0.038		0.0013
Muscle	0.016		0.00053
Kidney	0.437		0.0146
Liver	0.057		0.0019

[1] Calculated from the maximum residues observed at the dose level closest to the RBDB divided by the dose level.

Table 15. Expected Secondary Residues in Meat and Milk.				
Matrix	Dietary burden (ppm)	Secondary Residues (ppm)[1]	Proposed Tolerance (ppm)	Recommended Tolerance (ppm)[2]
Milk	1.0	0.00037	-	NR
Fat	1.2	0.0016	0.01	NR
Kidney		0.018	0.02[3]	0.02
Muscle		0.00064	0.01	NR
Liver		0.0023	0.01	NR

[1] Calculated from dietary burden x transfer coefficient from Table 14.
[2] NR = not required. However, HED is recommending for LOQ-level tolerances in order to harmonize with Canada.
[3] Meat byproducts, except liver.

Conclusions: The residue data from the cattle feeding studies are adequate to satisfy data requirements. The feeding study data indicate that tolerances are needed for the combined residues of spirotetramat and its metabolite BYI 08330-enol at 0.02 ppm in the kidney of cattle,

goats, horses, and sheep. Tolerances for milk, fat, meat byproducts (except kidney), and meat are not needed. However, HED is recommending for LOQ-level tolerances (0.02 ppm for fat, meat byproducts, and meat and 0.01 ppm for milk) in order to harmonize with Canada. As none of the proposed target crops are considered as a commodity for swine feed, tolerances for hogs are not needed.

Poultry feeding study waiver request

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

860.1500 Crop Field Trials

Brassica Leafy Vegetables

DER Reference List 46904509.der.doc

A total of 20 field trials were conducted in the U.S. to evaluate the magnitude of spirotetramat residues in/on representative commodities of broccoli/cauliflower and cabbage in crop subgroup 5A (head and stem *Brassica*) and mustard greens in crop subgroup 5B (leafy *Brassica* greens) following two broadcast foliar applications of either BYI 08330 100 OD formulation or BYI 08330 240 SC formulation.

A total of 12 field trials were conducted in crop subgroup 5A, including three broccoli trials, three cauliflower trials, and six cabbage trials. A decline trial was conducted with both broccoli and cabbage. Eight field trials were conducted in crop subgroup 5B with mustard greens, including a single decline trial.

BYI 08330 100 OD or BYI 08330 240 SC were applied at target rates of 88 g a.i./ha/application (0.078 lb a.i./A/application) at intervals of 5-7 days. Total seasonal application rates for all trials ranged from 171-184 g a.i./ha (0.153-0.164 lb a.i./A, 1X) for BYI 08330 100 OD and from 174-176 g a.i./ha (0.155-0.157 lb a.i./A, 1X) for BYI 08330 240 SC. All applications were made using spray volumes of 11 to 20 GPA (102 to 188 L/ha) and Dyne-Amic (a blend of highly refined methylated vegetables oils in combination with organosilicone-based surfactants, 0.5% v/v) as an additive.

The total residue of spirotetramat and the metabolites were quantitated by HPLC-MS/MS method 00857 using isotopically labeled internal standards. Method validation was performed prior to sample analysis and concurrent recoveries were performed during sample analysis to demonstrate acceptable method performance. The individual analyte residues of spirotetramat (parent) and the metabolites BYI 08330-enol, BYI 08330-ketohydroxy, BYI 08330-mono-hydroxy and BYI 08330-enol-Glc, were summed to give a total spirotetramat residue in parent equivalents. The LOQ was 0.01 ppm for each analyte in the RACs. The maximum storage interval of crop samples from harvest to analysis for total spirotetramat-derived residues was 518 days (17 months), 600 days (20 months), and 646 days (22 months) for broccoli, cauliflower, and cabbage samples, respectively. Total spirotetramat residues have been demonstrated to be stable for up to 718 days (months).

The maximum total spirotetramat residue (consisting of total residues of spirotetramat, BYI 08330-enol, BYI 08330-ketohydroxy, BYI 08330-mono-hydroxy and BYI 08330-enol-Glc) in/on broccoli/cauliflower (representative of head and stem *Brassica* from crop subgroup 5A) treated with BYI 08330 100 OD and harvested at 1-day PHI, 3-day PHI, and 7-day PHI was 0.45 ppm, 0.78 ppm, and 0.87 ppm, respectively. The maximum total spirotetramat residue in/on broccoli/cauliflower treated with BYI 08330 240 SC and harvested at 1-day PHI, 3-day PHI, and 7-day PHI was 0.32 ppm, 0.49 ppm, and 0.84 ppm, respectively. No clear decline of total spirotetramat residue was observed in the broccoli decline trial as total spirotetramat residue remained essentially the same at each sampling interval.

The maximum total spirotetramat residue in/on cabbage (representative of head and stem *Brassica* from crop subgroup 5A) with wrapper leaves intact treated with BYI 08330 100 OD and harvested at 1-day PHI, 3-day PHI, and 7-day PHI was 0.92 ppm, 0.52 ppm, and 0.45 ppm, respectively. Total spirotetramat residues in cabbage without wrapper leaves treated with the 100 OD formulations and harvested at a 1-day, 3-day, and 7-day PHI were 0.17 ppm, 0.17 ppm and 0.219 ppm. The maximum total spirotetramat residue in/on cabbage (with wrapper leaves) treated with BYI 08330 240 SC and harvested at 1-day PHI, 3-day PHI, and 7-day PHI was 0.05 ppm, 0.06 ppm, and 0.06 ppm, respectively. Maximum total residues in cabbages without wrapper leaves treated with the 240 SC formulation and harvested at a 1-day, 3-day and 7-day PHI were 0.056 ppm, 0.057 ppm and 0.060 ppm, respectively. No clear decline of total spirotetramat residue was observed in the cabbage decline trials as total spirotetramat residue remained the same at each sampling interval.

The maximum total spirotetramat residue in/on mustard greens (representative of Leafy *Brassica* Greens from Crop Subgroup 5B) treated with BYI 08330 100 OD and harvested at 1-day PHI, 3-day PHI, and 7-day PHI was 5.49 ppm, 4.61 ppm, and 5.60 ppm, respectively. The maximum total spirotetramat residue in/on mustard greens treated with BYI 08330 240 SC and harvested at 1-day PHI, 3-day PHI, and 7-day PHI was 4.46 ppm, 2.88 ppm, and 0.59 ppm, respectively.

TABLE 16. Summary of Residue Data from *Brassica* Leafy Vegetables Crop Field Trials.

Proposed Use Pattern: Two foliar sprays at 0.08 lb a.i./A/application with a minimum RTI of 7 days, for a maximum seasonal rate of 0.16 lb a.i./A and a PHI of 1 day.

Commodity	Total Applic. Rate (lb a.i./A) (kg a.i./ha)	PHI (days)	Total Spirotetramat Residue Levels[1] (ppm)						
			n	Min.	Max.	HAFT[2]	Median	Mean	Std. Dev.
Broccoli/Cauliflower									
Flower head and stems	100OD 0.154- 0.158 (0.173 - 0.177)	1	13	0.099	0.451	0.423	0.369	0.336	0.110
		3	12	0.134	0.782	0.762	0.370	0.383	0.209
		7	12	0.166	0.871	0.825	0.476	0.459	0.225
	240 SC 0.157 (0.176)	1	4	0.210	0.325	0.307	0.289	0.278	0.048
		3	4	0.225	0.490	0.411	0.279	0.318	0.125
		7	4	0.144	0.835	0.754	0.414	0.452	0.355
Cabbage									
Heads with wrapper leaves	100OD 0.154- 0.158 (0.173 - 0.177)	1	12	0.054	0.924	0.911	0.312	0.394	0.317
		3	12	0.063	0.515	0.480	0.226	0.255	0.140
		7	12	0.061	0.449	0.427	0.179	0.200	0.119
	240 SC 0.157	1	2	0.050	0.050	0.050	0.050	0.050	NA
		3	2	0.050	0.056	0.054	0.053	0.053	NA

TABLE 16. Summary of Residue Data from *Brassica* Leafy Vegetables Crop Field Trials.									
Proposed Use Pattern: Two foliar sprays at 0.08 lb a.i./A/application with a minimum RTI of 7 days, for a maximum seasonal rate of 0.16 lb a.i./A and a PHI of 1 day.									
	(0.176)	7	2	0.051	0.056	0.050	0.054	0.054	NA
Heads without wrapper leaves	100OD 0.154- 0.158 (0.173 - 0.177)	1	10	0.052	0.170	0.164	0.095	0.097	0.041
		3	10	0.057	0.171	0.163	0.131	0.115	0.046
		7	10	0.056	0.219	0.205	0.114	0.120	0.059
	240 SC 0.157 (0.176)	1	2	0.055	0.056	0.056	0.056	0.056	NA
		3	2	0.052	0.057	0.055	0.055	0.055	NA
		7	2	0.054	0.060	0.057	0.057	0.057	NA
Mustard Greens									
Greens	100 OD 0.153- 0.164 (0.171 - 0.184)	1	17	0.771	5.490	5.358	3.378	2.795	1.708
		3	16	0.687	4.618	4.347	2.507	2.515	1.302
		7	16	0.245	5.598	4.791	1.153	1.442	1.428
	240 SC 0.153 - 0.157 (0.174 -0.176)	1	4	0.784	4.460	4.400	2.600	2.611	2.066
		3	4	0.720	2.875	2.604	1.541	1.669	1.102
		7	4	0.351	0.593	0.592	0.484	0.478	0.132

[1] For the purpose of calculating total spirotetramat residues, individual analyte residues that were reported as <LOQ were assigned a finite value of LOQ.
[2] HAFT = Highest-Average Field Trial.

Conclusions: The submitted residue data for *Brassica* leafy vegetables are adequate to fulfill data requirements. The number and locations of the crop field trials are in accordance with OPPTS Guideline 860.1500 (Table 17). The available data will support the proposed use pattern.

TABLE 17. Trial Numbers and Geographical Locations for *Brassica* Leafy Vegetables.									
NAFTA Growing Zones	Broccoli/Cauliflower			Cabbage			Mustard Greens		
	Submitted	Requested*		Submitted	Requested*		Submitted	Requested*	
		Canada	U.S.		Canada	U.S.		Canada	U.S.
1				1		1			
2				1		1	2		2
3				1		1	1		1
4							1		1
5		2		1	2	1	1		1
5B		2			2				
6	1		1	1		1	1		1
10	4		4	1		1	2		2
12	1	1	1		1				
Total	6	5	6	6	5	6	8		8

* Number for crop group request.

The residue data for cabbage field (heads with wrapper leaves, 100 OD formulation) and mustard greens (100 OD formulation) were entered into the Agency's tolerance spreadsheet as specified by the *Guidance for Setting Pesticide Tolerances Based on Field Trial Data* SOP to determine appropriate tolerance levels; see Appendix II. The recommended tolerances for the combined residues of spirotetramat, BYI 08330-enol, BYI 08330-ketohydroxy, BYI 08330-mono-hydroxy and BYI 08330-enol-Glc, expressed as parent equivalents, are 2.5 ppm for *Brassica,* head and stem, subgroup 5A; and 8.0 ppm for *Brassica*, leafy greens, subgroup 5B.

Citrus

DER Reference List 46904514.der.doc

During the 2005 growing season, 12 orange, 5 lemon and 6 grapefruit trials were conducted in the U.S. covering NAFTA Zones 3 (FL; 8 trials), 6 (TX; 1 trial) and 10 (CA; 3 trials) for orange; Zones 3 (FL; 1 trial) and 10 (CA; 4 trials) for lemons; and Zones 3 (FL; 3 trials), 6 (TX; 1 trial), 10 (CA; 2 trials) for grapefruit.

Two ground-based airblast spray applications of either BYI 08330 150 OD or BYI 08330 240 SC were made at each trial location. Applications were made at rates that ranged from 0.150 to 0.166 lb a.i./A/application (0.168 to 0.187 kg a.i./ha/application), for a total seasonal rate of from 0.306 to 0.321 lb a.i./A/season (0.344 to 0.360 kg a.i./ha/season, 1X). The RTIs ranged from 14 to 21 days. All spray mixtures included Dyne-Amic adjuvant (0.25% v/v).

Citrus fruit were harvested at a PHI of 1 day. In the decline trials (one orange, one lemon, and one grapefruit), samples were collected at five intervals (±1 day) corresponding to PHIs of 0, 1, 7, 10, and 14 days. Additional orange samples were collected to determine the possible reduction of total spirotetramat residue after removing the peel from orange whole fruit.

Residues of spirotetramat and its metabolites BYI 08330 cis-enol, BYI 08330 ketohydroxy, BYI 08330 monohydroxy, and BYI 08330 enol-Glc were analyzed by HPLC-MS/MS using radiolabeled internal standards. The LOQ for each analyte was 0.050 ppm in all matrices. The calculated LOD values for spirotetramat, BYI 08330-enol, BYI 08330-keto-hydroxy, BYI 08330-mono-hydroxy, BYI 08330-enol-Glc and total spirotetramat were 0.041 ppm, 0.006 ppm, 0.006 ppm, 0.006 ppm, 0.006 ppm and 0.041 ppm, respectively.

The orange, lemon, and grapefruit samples analyzed in this study were held in frozen storage for a maximum of 13.5 months prior to analysis. Based on the storage stability report, total spirotetramat residues are expected to be stable for up to 24 months. Therefore, the length of frozen storage of citrus commodities would not affect the magnitude of total spirotetramat residues observed.

Total residue levels were marginally higher with the BYI 08330 150 OD formulation than with the BYI 08330 240 SC formulation, and spirotetramat appeared to be metabolized or degraded to a greater extent with the BYI 08330 150 OD formulation. In decline trials, detectable residues dissipated with increasing PHIs in orange and grapefruit, but not in lemon.

Maximum residue levels in/on **orange** were 0.213 ppm (spirotetramat), 0.148 ppm (BYI 08330 cis-enol), 0.077 ppm (BYI 08330 cis-keto-hydroxy), 0.050 ppm (BYI 08330 mono-hydroxy), 0.050 ppm (BYI 08330 enol-Glc), and 0.433 (total spirotetramat). The maximum residue levels in/on **lemon** were 0.199 ppm (spirotetramat), 0.159 ppm (BYI 08330 cis-enol), 0.050 ppm (BYI 08330 cis-keto-hydroxy), 0.050 ppm (BYI 08330 mono-hydroxy), 0.050 ppm (BYI 08330 enol-Glc), and 0.465 ppm (total spirotetramat). The maximum residue levels in/on **grapefruit** were 0.151 ppm (spirotetramat), 0.063 ppm (BYI 08330 cis-enol), 0.050 ppm (BYI 08330 cis-keto-hydroxy), 0.050 ppm (BYI 08330 mono-hydroxy), 0.050 ppm (BYI 08330 enol-Glc), and 0.351 ppm (total spirotetramat). Most residues in orange appeared to be associated with the peel because when it was removed, total spirotetramat residues levels decreased to below the LOQ.

TABLE 18. Summary of Residue Data from Citrus Field Trials.

Proposed Use Pattern: Two foliar sprays at 0.16 lb a.i./A/application with a minimum RTI of 21 days, for a maximum seasonal rate of 0.32 lb a.i./A and a PHI of 1 day.

Residue	Total App. Rate lb a.i./A (kg a.i./ha)	App. Method	PHI (days)	Residue Levels (ppm)[1]						
				n	Min	Max	HAFT[2]	Median	Mean	Std. Dev.
Orange (150 OD Formulation)										
Total Spirotetramat	0.306–0.321 (0.344–0.360)	Conc. Spray	1	27	0.250	0.433	0.427	0.319	0.324	0.06
		Dil. Spray		24	0.250	0.375	0.361	0.288	0.285	0.04
Orange (240 SC Formulation)										
Total Spirotetramat	0.306–0.321 (0.344–0.360)	Conc. Spray	1	6	0.250	0.413	0.388	0.307	0.315	0.06
Lemon (150 OD Formulation)										
Total Spirotetramat	0.306–0.321 (0.344–0.360)	Conc. Spray	1	10	0.274	0.465	0.456	0.315	0.337	0.07
		Dil. Spray		10	0.251	0.427	0.397	0.292	0.304	0.06
Lemon (240 SC Formulation)										
Total Spirotetramat	0.306–0.321 (0.344–0.360)	Conc. Spray	1	2	0.305	0.392	0.348	—	—	—
Grapefruit (150 OD Formulation)										
Total Spirotetramat	0.306–0.321 (0.344–0.360)	Conc. Spray	1	12	0.250	0.351	0.345	0.250	0.265	0.04
		Dil. Spray		12	0.250	0.264	0.264	0.250	0.253	0.01
Grapefruit (240 SC Formulation)										
Total Spirotetramat	0.306–0.321 (0.344–0.360)	Conc. Spray	1	4	0.250	0.250	0.250	0.250	0.250	0

[1] For the purpose of calculating total spirotetramat residues, individual analyte residues that were reported as <LOQ were assigned a finite value of LOQ.
[2] HAFT = Highest-Average Field Trial.

Conclusions: The submitted field trial data for citrus are adequate to fulfill data requirements. The number and locations of the trials are in accordance with OPPTS Guideline 860.1500 (Table 19). The available data will support the proposed use pattern.

TABLE 19. Trial Numbers and Geographical Locations for Citrus.

NAFTA Growing Zones	Orange		Lemon		Grapefruit	
	Submitted	Requested NAFTA	Submitted	Requested NAFTA	Submitted	Requested NAFTA
3	8	8	1	1	3	3
6	1	1			1	1
10	3	3	4	4	2	2
Total	12	12	5	5	6	6

The residue data for lemons (concentrated spray, 100 OD formulation) were entered into the Agency's tolerance spreadsheet as specified by the *Guidance for Setting Pesticide Tolerances Based on Field Trial Data* SOP to determine appropriate tolerance levels; see Appendix II. The recommended tolerance for the combined residues of spirotetramat, BYI 08330-enol, BYI 08330-ketohydroxy, BYI 08330-mono-hydroxy and BYI 08330-enol-Glc, expressed as parent equivalents, is 0.60 ppm for fruit, citrus, group 10.

Cucurbit Vegetables

DER Reference List 46904511.der.doc

A total of 17 field trials were conducted in the U.S. to evaluate the magnitude of spirotetramat residues in/on cucumber (6 trials), muskmelon (6 trials) and summer squash (5 trials) following two broadcast foliar applications of either BYI 08330 100 OD or BYI 08330 240 SC. All trials had one plot sprayed with BYI 08330 100 OD; at least one trial for each representative commodity had an additional bridging plot treated with BYI 08330 240 SC. Each formulation was applied at a rate of 0.081-0.093 kg a.i./ha/application (0.072 to 0.083 lb a.i./A/application) for BYI 08330 100 OD and 0.085-0.090 kg a.i./ha/application (0.076 to 0.081 lb a.i./A/ application) for BYI 08330 240 SC. The interval between the two applications ranged from 5 to 7 days for BYI 08330 100 OD and from 6 to 7 days for BYI 08330 240 SC. Total seasonal application rates for all trials ranged from 0.165 to 0.181 kg a.i./ha (0.147 to 0.161 lb a.i./A, 1X) for BYI 08330 100 OD and from 0.173 to 0.179 kg a.i./ha (0.154 to 0.160 lb a.i./A, 1X) for BYI 08330 240 SC. All spray mixtures included Dyne-Amic adjuvant.

Samples of cucumber, muskmelon, and summer squash were harvested at earliest crop maturity at PHIs of 1-day. In all trials, single control samples and duplicate treated samples were collected for all matrices. Additional samples were harvested to investigate the decline of residues with time. In the decline trials, the samples were collected at five intervals corresponding to PHIs of ~0, 1, 3, 7 and 10 days.

The residues of spirotetramat and the metabolites BYI 08330-enol, BYI 08330-ketohydroxy, BYI 08330-mono-hydroxy, and BYI 08330-enol-Glc were quantitated by method 00857. The individual analyte residues were converted to spirotetramat molar equivalents and summed to give total spirotetramat residues. The LOQ for each analyte was reported as 0.01 ppm in cucumber, muskmelon and summer squash. Adequate method-validation data were provided. The cucumber, muskmelon and summer squash samples were stored frozen for a maximum of 23.6 months (708 days) prior to analysis. Total spirotetramat residues are stable for up to 24 months (718 days) in plant matrices.

The total spirotetramat residues in cucumber, muskmelon and summer squash were similar in plots treated with BYI 08330 100 OD as compared with the bridging plots treated with BYI 08330 240 SC for all matrices. At the PHI of 1 day, the maximum total spirotetramat residues in cucumber, muskmelon and summer squash treated with the 100 OD formulation were 0.076 ppm, 0.134 ppm and 0.184 ppm, respectively.

TABLE 20. Summary of Residue Data from Cucurbit Vegetable Crop Field Trials.

Proposed Use Pattern: Two foliar sprays at 0.08 lb a.i./A/application with a minimum RTI of 7 days, for a maximum seasonal rate of 0.16 lb a.i./A and a PHI of 1 day.

Commodity	Total Applic. Rate lb a.i./A (kg a.i./ha)	PHI (days)	Residue Levels1 (ppm)						
			n	Min.	Max.	HAFT[2]	Median	Mean	Std. Dev.
Cucumber-100 OD	0.147-0.161 (0.165-0.181)	1	12	<0.050	0.076	0.075	0.050	0.057	0.011
Cucumber-240 SC	0.154-0.160 (0.173-0.179)	1	4	<0.050	0.057	0.054	0.050	0.052	0
Muskmelon-100 OD	0.147-0.161 (0.165-0.181)	1-2	12	<0.050	0.134	0.098	0.054	0.063	0.024
Muskmelon-240 SC	0.154-0.160 (0.173-0.179)	1-2	4	<0.050	0.163	0.113	0.060	0.083	0.053
Summer Squash 100 OD	0.147-0.161 (0.165-0.181)	1	10	<0.050	0.184	0.173	0.069	0.095	0.051
		3	10	<0.050	0.161	0.132	0.066	0.081	0.037
		7	10	<0.050	0.067	0.059	0.050	0.052	0.005
Summer Squash 240 SC	0.154-0.160 (0.173-0.179)	1	2	<0.050	0.051	0.051	--	--	--
		3	2	<0.050	<0.050	--	--	--	--
		7	2	<0.050	<0.050	--	--	--	--

[1] For the purpose of calculating total spirotetramat residues, individual analyte residues that were reported as <LOQ were assigned a finite value of LOQ.
[2] HAFT = Highest-Average Field Trial.
-- Not applicable.

Conclusions: The submitted field trial data for cucurbit vegetables are adequate to fulfill data requirements. The number and locations of the trials are in accordance with OPPTS Guideline 860.1500 (Table 21). The available data will support the proposed use pattern.

TABLE 21. Trial Numbers and Geographical Locations for Cucurbit Vegetables.

NAFTA Growing Zones	Cucumber			Muskmelon			Summer Squash		
	Submitted	Requested		Submitted	Requested		Submitted	Requested	
		Canada	U.S.		Canada	U.S.		Canada	U.S.
1							1		1
1A								1	
2	2		2	1		1	1		1
3	1		1				1		1
5	2	2	2	1	2	1	1	2	1
5B		2			1			1	
6	1		1	1		1			
10				3		3	1		1
12		2						1	
Total	6		6	6		6	5		5

The residue data for summer squash (100 OD formulation) were entered into the Agency's tolerance spreadsheet as specified by the *Guidance for Setting Pesticide Tolerances Based on Field Trial Data* SOP to determine appropriate tolerance levels; see Appendix II. The recommended tolerance for the combined residues of spirotetramat, BYI 08330-enol, BYI 08330-ketohydroxy, BYI 08330-mono-hydroxy and BYI 08330-enol-Glc, expressed as parent equivalents, is 0.30 ppm for vegetable, cucurbit, group 9.

Fruiting Vegetables

DER Reference List 46904510.der.doc

Bayer Cropscience has submitted field trial data for spirotetramat on tomatoes, bell peppers and non-bell (chili) peppers as representative commodities for crop group 8, the fruiting vegetables. A total of 21 trials were conducted in the U.S. encompassing NAFTA zones 1 (1 trial), 2 (VA, PA, GA; 3 trials), 3 (FL; 4 trials), 5 (NE, KS; 2 trials), 6 (TX; 1 trial) and 10 (CA; 10 trials) during the 2004 growing season.

At each trial location, two broadcast foliar applications of BYI 08330 100 OD or BYI 08330 240 SC were made to tomatoes, bell peppers, or non-bell peppers at a target rate of 0.0785 lb a.i./A/application (88 g a.i./ha/application) for a total seasonal rate that ranged from 0.150 to 0.178 lb a.i./A (0.168 to 0.199 kg a.i./ha, ~1X). RTIs were 5 to 7 days. All spray mixtures included Dyne-Amic adjuvant.

In total, twelve trials were conducted on tomatoes (11 harvest and 1 decline), six trials were conducted on bell pepper (5 harvest and 1 decline) and three trials were conducted on non-bell or non-bell pepper (3 harvest) with nominal PHIs of 1, 3, and 7 days. In decline trials, samples were collected at nominal PHIs of 0, 1, 3, 7 and 10 days.

Residues of spirotetramat and the metabolites BYI 08330 cis-enol, BYI 08330 ketohydroxy, BYI 08330 monohydroxy, and BYI 08330 enol-Glc were analyzed by HPLC-MS/MS using radiolabeled internal standards. The LOQ was 0.010 ppm for each analyte in all three fruiting vegetables examined. The calculated LODs, expressed in parent equivalents, for spirotetramat (parent), BYI 08330-enol, BYI 08330-ketohydroxy, BYI 08330-mono-hydroxy and BYI 08330-enol-Glc were 0.0031 ppm, 0.0035 ppm, 0.0049 ppm, 0.0034 ppm and 0.0036 ppm for tomatoes; 0.0037 ppm, 0.0059 ppm, 0.0040 ppm, 0.0052 ppm and 0.0030 ppm for bell peppers; 0.0020 ppm, 0.0077 ppm, 0.0029 ppm, 0.0038 ppm, and 0.0020 ppm for non-bell peppers. Maximum total residues were 6.1X higher in non-bell peppers than in tomatoes and 2.1X higher in non-bell peppers than in bell peppers.

The fruiting vegetable samples analyzed in this study were held in frozen storage for a maximum 678 days prior to analysis. Based on a storage stability study, total spirotetramat residues are stable for up to 718 days.

Total spirotetramat residue levels were higher with the BYI 08330 100 OD formulation than with the BYI 08330 240 SC formulation. Additionally, spirotetramat appeared to be metabolized/degraded to a greater extent with the BYI 08330 100 OD formulation.

With a 1-day PHI, the maximum residue levels in/on tomato were 0.088 ppm (spirotetramat), 0.165 ppm (BYI 08330-enol), 0.022 ppm (BYI 08330-ketohydroxy), 0.010 ppm (BYI 08330-mono-hydroxy), 0.016 ppm (BYI 08330-enol-Glc), and 0.227 ppm (total spirotetramat); the maximum residue levels in/on bell peppers were 0.046 ppm (spirotetramat), 0.530 ppm (BYI 08330-enol), 0.139 ppm (BYI 08330-ketohydroxy), 0.010 ppm (BYI 08330-mono-hydroxy), 0.022 ppm (BYI 08330-enol-Glc), and 0.682 ppm (total spirotetramat); the maximum residue levels in/on non-bell peppers were 0.088 ppm (spirotetramat), 1.12 ppm (BYI 08330-enol), 0.143 ppm (BYI 08330-ketohydroxy), 0.010 ppm (BYI 08330-mono-hydroxy), 0.022 ppm (BYI 08330-

enol-Glc), 1.38 ppm (total spirotetramat).

No clear decline of total spirotetramat residue was observed in the tomato and pepper decline trials as total spirotetramat residues remained approximately the same at each sampling interval, suggesting that spirotetramat and metabolites are persistent over the time frame studied.

In the additional processed bell pepper samples which were washed, peeled and cooked by boiling, a slight concentration of total spirotetramat residue was found in washed peppers (1.3X) and cooked peppers (1.2X).

TABLE 22. Summary of Residue Data from Fruiting Vegetable Field Trials.

Proposed Use Pattern: Two foliar sprays at 0.08 lb a.i./A/application with a minimum RTI of 7 days, for a maximum seasonal rate of 0.16 lb a.i./A and a PHI of 1 day.

Commodity and Formulation	Total App. Rate lb a.i./A (kg a.i./ha)	PHI (days)	Residue Levels (ppm)[1]						
			n	Min	Max	HAFT[2]	Median	Mean	Std. Dev.
Tomato OD	0.150–0.178 (0.168–0.199)	1	24	0.060	0.227	0.214	0.137	0.139	0.049
		3	24	0.059	0.235	0.204	0.141	0.138	0.051
		7	24	0.057	0.306	0.264	0.162	0.173	0.073
Tomato SC	0.150–0.178 (0.168–0.199)	1	6	0.072	0.189	0.177	0.139	0.130	0.048
		3	6	0.075	0.172	0.167	0.131	0.124	0.043
		7	6	0.064	0.235	0.230	0.142	0.148	0.071
Bell Pepper OD	0.150–0.178 (0.168–0.199)	1	12	0.156	0.682	0.655	0.299	0.351	0.182
		3	12	0.152	0.835	0.807	0.436	0.449	0.237
		7	12	0.199	1.070	0.850	0.432	0.507	0.264
Bell Pepper SC	0.150–0.178 (0.168–0.199)	1	4	0.188	0.361	0.275	0.259	0.267	0.080
		3	4	0.358	0.488	0.433	0.384	0.404	0.058
		7	4	0.361	0.390	0.390	0.387	0.381	0.014
Non-Bell Pepper OD	0.150–0.178 (0.168–0.199)	1	6	0.427	1.379	1.232	0.558	0.748	0.390
		3	6	0.552	0.883	0.871	0.762	0.747	0.124
		7	6	0.588	1.471	1.207	0.933	0.934	0.303

[1] For the purpose of calculating total spirotetramat residues, individual analyte residues that were reported as <LOQ were assigned a finite value of LOQ.
[2] HAFT = Highest-Average Field Trial.

Conclusions: The submitted field trial data for fruiting vegetables are adequate to fulfill data requirements. The number and locations of the trials are in accordance with OPPTS Guideline 860.1500 (Table 23). The available data will support the proposed use pattern.

TABLE 23. Trial Numbers and Geographical Locations for Fruiting Vegetables.*

NAFTA Growing Zones	Tomatoes		Bell Pepper		Non-Bell Pepper	
	Submitted	NAFTA Requested	Submitted	NAFTA Requested	Submitted	NAFTA Requested**
1	1	1				
2	1	1	1	1	1	
3	2	2	1	1	1	
5	1	1	1	1		
6			1	1		
10	7	7	2	2	1	
Total	12	12	6	6	3	3

* Number for crop group request.
** Regions are not specified and ≤3 trials are required.

The residue data for non-bell peppers (100 OD formulation) were entered into the Agency's tolerance spreadsheet as specified by the *Guidance for Setting Pesticide Tolerances Based on Field Trial Data* SOP to determine appropriate tolerance levels; see Appendix II. The recommended tolerance for the combined residues of spirotetramat, BYI 08330-enol, BYI 08330-ketohydroxy, BYI 08330-mono-hydroxy and BYI 08330-enol-Glc, expressed as parent equivalents, is 2.5 ppm for, group 8. As okra is not officially part of the fruiting vegetable crop group, a separate tolerance of 2.5 ppm should be proposed for this commodity.

Grapes

DER Reference List 46904517.der.doc

During the 2005 growing season, 12 trials were conducted in the U.S. encompassing NAFTA zones 1 (PA, NY; 2 trials), 10 (CA, 8 trials), 11 (WA, OR; 2 trials). Nine trials had one plot sprayed with BYI 08330 150 OD and three trials had an additional plot treated with BYI 08330 240 SC. Each formulation was applied as a ground-based foliar spray at rates that ranged from 0.097 to 0.101 lb a.i./A/application (0.109 to 0.114 kg a.i./ha/application). The RTIs ranged from 28 to 30 days. Total seasonal application rates for all trials ranged from 0.195 to 0.203 lb a.i./A (0.219 to 0.227 kg a.i./ha, 1X). All applications were made in spray volumes of 49 to 70 GPA (458 to 654 L/ha) and used Dyne-Amic (0.25% v/v) as an adjuvant.

In all trials, single control samples and duplicate treated samples were collected for all matrices. In the harvest and bridging trials, grapes were harvested at normal maturity. Sampling was performed at two PHIs 7 and 14 days. In the decline trial, grapes were collected at five intervals corresponding to PHIs of 3, 7, 10, 14, and 21 days.

Residues of spirotetramat and its metabolites BYI 08330-enol, BYI 08330-ketohydroxy, BYI 08330-monohydroxy, and BYI 08330-enol-Glc were measured with method 00857 which uses HPLC-MS/MS and radiolabeled internal standards. The method was validated and has a LOQ of 0.010 ppm for each analyte. The calculated LODs were 0.0039 ppm for spirotetramat (parent), 0.0051 ppm for BYI 08330-enol, 0.0015 ppm for BYI 08330-ketohydroxy, 0.0039 ppm for BYI 08330-mono-hydroxy, and 0.0045 ppm for BYI 08330-enol-Glc.

The grapes analyzed in this study were held in frozen storage for a maximum of 281 days. A freezer storage stability study demonstrated that residues of total spirotetramat were stable for 718 days in a diverse set of crops.

Maximum total spirotetramat residue levels were approximately 2X higher with the BYI 08330 150 OD formulation than with the BYI 08330 240 SC formulation. Total residues of spirotetramat and its metabolites did not appear to dissipate as the PHI increased from 3 days to 21 days. At a PHI of 7 days, the maximum residue levels in/on grapes were 0.494 ppm (spirotetramat), 0.503 ppm (BYI 08330-enol), 0.206 ppm (BYI 08330-ketohydroxy), 0.046 ppm (BYI 08330-mono-hydroxy), 0.144 ppm (BYI 08330-enol-Glc), and 1.29 ppm (total spirotetramat).

TABLE 24. Summary of Residue Data from Grape Field Trials.

Proposed Use Pattern: Two foliar sprays at 0.08-0.12 lb a.i./A/application with a minimum RTI of 30 days, for a maximum seasonal rate of 0.20 lb a.i./A and a PHI of 7 days.

Commodity and Formulation	Total App. Rate lb a.i./A (kg a.i./ha)	PHI (days)	Residue Levels (ppm)[1]						
			n	Min	Max	HAFT	Median	Mean	Std. Dev.
Grape OD	0.195–0.203 (0.219–0.227)	7	24	0.109	1.290	1.024	0.329	0.406	0.257
		14	24	0.072	0.843	0.806	0.397	0.412	0.242
Grape SC	0.195–0.203 (0.219–0.227)	7	3	0.187	0.547	0.466	0.347	0.348	0.130
		14	6	0.245	0.393	0.332	0.272	0.295	0.060

[1] For the purpose of calculating total spirotetramat residues, individual analyte residues that were reported as <LOQ were assigned a finite value of LOQ.

Conclusions: The submitted field trial data for grapes are adequate to fulfill data requirements. The number and locations of the trials are in accordance with OPPTS Guideline 860.1500 (Table 25). The available data will support the proposed use pattern.

TABLE 25. Trial Numbers and Geographical Locations for Grapes.

NAFTA Growing Zones	Grapes	
	Submitted	NAFTA Requested
1	2	2
10	8	8
11	2	2
Total	12	12

The residue data for grapes (100 OD formulation) were entered into the Agency's tolerance spreadsheet as specified by the *Guidance for Setting Pesticide Tolerances Based on Field Trial Data* SOP to determine appropriate tolerance levels; see Appendix II. The recommended tolerance for the combined residues of spirotetramat, BYI 08330-enol, BYI 08330-ketohydroxy, BYI 08330-mono-hydroxy and BYI 08330-enol-Glc, expressed as parent equivalents, is 1.3 ppm for small fruit vine climbing subgroup, except fuzzy kiwifruit, subgroup 13-07F.

Hops

DER Reference List 46904518.der.doc

Three field trials were conducted in the U.S. in zone 11 (ID, OR, WA, 3 trials) during the 2005 growing season. At each trial location, BYI 08330 150 OD or BYI 08330 240 SC was applied twice as a postemergent foliar spray at a rate of 0.096 to 0.100 lb a.i./A/application (0.108 to 0.112 kg a.i./ha/application) with a RTI of 12 to 14 days. The total application rate was from 0.194 to 0.200 lb a.i./A/season (0.218 to 0.224 kg a.i./ha/season, 1X). All spray mixtures included Dyne-Amic (0.25% v/v) as an adjuvant. Hop cones were harvested at PHIs of 7 to 8 days and of 14 days.

Residues of spirotetramat and its metabolites BYI 08330-enol, BYI 08330-ketohydroxy, BYI 08330-mono-hydroxy, and BYI 08330-enol-Glc were analyzed by HPLC-MS/MS using radiolabeled analytes as internal standards. The LOQ was 0.100 ppm and the calculated LOD

was 0.001 ppm for each analyte.

The hops dried cones analyzed in this study were held in frozen storage for a maximum of 11 months (321 days) prior to extraction. Total spirotetramat residues are stable for up to 718 days.

Total spirotetramat residue levels were similar using the BYI 08330 150 OD formulation in comparison to the BYI 08330 240 SC formulation in the one bridging trial. Total spirotetramat residue levels decreased slightly when the PHI increased from 7 to 14 days.

The maximum residue levels in/on hop cones were 4.24 ppm (spirotetramat), 0.928 ppm (BYI 08330 cis-enol), 0.220 ppm (BYI 08330 cis-keto-hydroxy), 0.100 ppm (BYI 08330 mono-hydroxy), 0.663 ppm (BYI 08330 enol-Glc), and 5.82 ppm (total spirotetramat).

TABLE 26. Summary of Residue Data from Hops Field Trials.

Proposed Use Pattern: Two foliar sprays at 0.10 lb a.i./A/application with a minimum RTI of 14 days, for a maximum seasonal rate of 0.20 lb a.i./A and a PHI of 7 days.

Commodity and Formulation	Total App. Rate lb a.i./A (kg a.i./ha)	PHI (days)	Residue Levels (ppm)[1]						
			n	Min	Max	HAFT[2]	Median	Mean	Std. Dev.
Hops OD	0.194–0.200 (0.218–0.224)	7	6	2.164	5.820	5.492	5.167	4.427	1.675
		14	6	2.571	5.368	5.164	4.604	4.147	1.182
Hops SC	0.194–0.200 (0.218–0.224)	7	2	3.149	4.512	3.830	—	3.830	—
		14	2	2.943	3.193	3.068	—	3.068	—

[1] For the purpose of calculating total spirotetramat residues, individual analyte residues that were reported as <LOQ were assigned a finite value of LOQ.
[2] HAFT = Highest-Average Field Trial.

Conclusions: The submitted field trial data for hops are adequate to fulfill data requirements. The number and locations of the trials are in accordance with OPPTS Guideline 860.1500 (Table 27). The available data will support the proposed use pattern.

TABLE 27. Trial Numbers and Geographical Locations.

NAFTA Growing Zones	Hops	
	Submitted	NAFTA Requested
11	3	3
Total	3	3

The residue data for hops (100 OD formulation) were entered into the Agency's tolerance spreadsheet as specified by the *Guidance for Setting Pesticide Tolerances Based on Field Trial Data* SOP to determine appropriate tolerance levels; see Appendix II. The recommended tolerance for the combined residues of spirotetramat, BYI 08330-enol, BYI 08330-ketohydroxy, BYI 08330-mono-hydroxy and BYI 08330-enol-Glc, expressed as parent equivalents, is 10 ppm for hop, dried cones.

Leafy Vegetables

DER Reference List 46904508.der.doc

A total of 24 field trials were conducted in the U.S. to measure the magnitude of spirotetramat residues in leafy vegetables following two broadcast foliar applications of either BYI 08330 100