UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF CHEMICAL SAFETY
AND POLLUTION PREVENTION

MEMORANDUM

Date: 12-FEB-2021

Subject: **Spinosad and Spinetoram.** Proposed Use on Dragon Fruit (Pitaya); Crop Group Expansion for Berry, Low Growing, Except Strawberry, Subgroup 13-07H; and Crop Group Conversions for Vegetable, *Brassica*, Head and Stem, Group 5-16; *Brassica*, Leafy Greens, Subgroup 4-16B; Leaf Petiole Vegetable Subgroup 22B; Leafy Greens Subgroup 4-16A; Celtuce; Fennel, Florence, Fresh Leaves and Stalk; and Kohlrabi. **Summary of Analytical Chemistry and Residue Data**

PC Codes: Spinetoram - 110007, 110008, 110009; Spinosad - 110003	**DP Barcode:** D461043
Decision No.: 553271	**Registration Nos.:** 62719-541; 62719-545, 62719-671
Petition No.: 9E8763	**Regulatory Action:** Section 3 Registration
Risk Assessment Type: NA	**Case Nos.:** Spinosad - 7421; Spinetoram - 7448
TXR No.: NA	**CAS Nos.:** Spinosad - 131929-60-7; Spinetoram - 935545-74-7, 187166-40-1 and 187166-15-0
MRID No.: 50854301	**40 CFR:** Spinosad - 180.495; Spinetoram - 180.635

Reviewer: Oluwaseun Gbemigun, Ph.D., Chemist
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Through: George F. Kramer, Ph.D., Senior Chemist
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RAB1/HED; 7509P

To: Nancy Fitz, RM05
Registration Division (RD; 7505P)

Summary of Submitted/Reviewed Residue Chemistry Studies

OCSPP Guideline	Reference
860.1500	MRID 50854301. Barney, W.P. (2017) Spinetoram: Magnitude of the Residue on Dragon Fruit (Pitaya). Study Numbers: 11514; 11514.15-FLR09. Unpublished study prepared and submitted by Interregional Research Project Number 4. 197 p.

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1.0 Executive Summary

Background: Spinosad, which consists of spinosyn A and spinosyn D (A:D of 85:15), is a fermentation product of *Saccharopolyspora spinosad*. Spinetoram, which consists of XDE-175-J and XDE-175-L (J:L of 3:1), is derived from the synthetic modification of *Saccharopolyspora spinosa* fermentation products. Spinosad and spinetoram are structurally similar with both registered for application to numerous crops for control of foliage-feeding pests including lepidoptera larvae (worms or caterpillars), Colorado potato beetles, dipterous leafminers, thrips, and/or certain psyllids. The insecticidal mode of action for both spinosad and spinetoram involves disruption of the nicotinic acetylcholine receptors.

Proposed Use: The Interregional Research Project No. 4 (IR-4) requested Section 3 Registrations of spinosad and spinetoram on dragon fruit (pitaya). In addition, IR-4 is also requesting a crop group expansion for Berry, low growing, except strawberry, subgroup 13-07H; Celtuce, Fennel, Florence, fresh leaves and stalk, Kohlrabi, Leaf petiole vegetable subgroup 22B, Vegetable, *Brassica*, head and stem, group 5-16, and Vegetable, leafy, group 4-16.

Table 3.3.1 is a summary of the end-use products and Table 3.3.2 is a summary of the proposed application scenarios. HED concludes that the proposed application scenarios are supported by the available residue chemistry data.

Nature of the Residue: The nature of spinosad and spinetoram residues in primary crops, rotational crops, and livestock is adequately understood. Tables 4.0.1 and 4.0.2 are summaries of the residues of concern for tolerance enforcement and risk assessment purposes. No additional metabolism/rotational crop data are required to support the current requests.

Magnitude of the Residue - Primary Crops: HED concludes that the available magnitude of the residue data are adequate and support the HED recommended tolerances listed in Table 2.2.2. EPA previously concluded that the translation of spinosad residue data to spinetoram for crops was acceptable due to the similar chemical structures, similar residue levels for similar application rates. Translation of spinosad processing factors to spinetoram has also been deemed acceptable (EPA, D325387, T. Bloem, 12-SEP-2007).

Magnitude of the Residue – Rotational Crops: Based on the results of a spinosad confined rotational crop study and the proposed application rates, HED concludes that no rotational crop restrictions or tolerances are required for the currently-proposed crops (D243816, G. Herndon, 03-MAR-1998). Field rotational crop data have not been submitted and are not required.

Based on the results of a spinetoram confined rotational crop study and the proposed application rates, HED concludes that the proposed 30-day plant-back interval (PBI) for all nonlabeled crops is appropriate (46695021.der.doc; 47396301.der.doc).

Magnitude of the Residue - Livestock: HED concludes that the currently established tolerances for residues in/on livestock commodities are adequate to cover all registered/proposed uses.

HED concludes that the residue chemistry database is adequate to support the proposed

application scenarios and establishment of the tolerances listed in Section 2.2.2. A human health risk assessment will be prepared as a separate document (D454564, J. Tyler, 02-MAR-2021).

2.0 HED Recommendation

HED concludes that the residue chemistry database is adequate to support the proposed application scenarios and establishment of the tolerances listed in Section 2.2.2. A human health risk assessment will be prepared as a separate document (D454564, J. Tyler, 02-MAR-2021).

2.1 Data Deficiencies/Data Needs

None

2.2 Tolerance Considerations

2.2.1 Enforcement Analytical Method

Spinosad: The following is a summary of the methods available for enforcement of the spinosad tolerances.

Plants: Method RES 94025 (GRM 94.02) is a HPLC/UV method which was originally submitted for the determination of spinosyn A and D in/on cottonseed and related commodities (LOQ = 0.01 ppm for spinosyn A and D). The method was successfully subjected to an ILV as well as an EPA laboratory validation and has been forwarded to FDA for tolerance enforcement (D228791, G. Herndon, 13-AUG-1996). The following additional methods have also been determined to be adequate for tolerance-enforcement purposes and were submitted to FDA (LOQ = 0.01 ppm for all; D242940, G. Herndon, 18-FEB-1998; D237752, G. Herndon, 02-MAR-1998; D232203, G. Herndon, 02-MAR-1998; D243795, G. Herndon, 02-MAR-1998):

Since the dragon fruit magnitude of the residue data submitted support of the current petition were generated using an immunoassay method very similar to the current enforcement method GRM 96.16 and since the magnitude of the residue study included adequate validation data, HED concludes that the current enforcement method is suitable for enforcement of the spinetoram dragon fruit tolerances recommended herein. The remaining recommended tolerances reflect an update to the current crop group/subgroup commodity definitions and, therefore, the current enforcement methods are sufficient.

Livestock: Method RES 95114, an immunoassay method for determination of spinosad residues in ruminant and hog commodities which underwent a successful ILV and EPA laboratory validation and has been submitted to FDA for tolerance enforcement (D245206, G. Herndon, 5-JAN-1999). Method GRM 95.15 is a HPLC/UV has been determined to be sufficient for enforcement of the currently established poultry tolerances (D249374, M. Doherty, 24-JUN-1999).

Spinetoram: The following is a summary of the methods available for enforcement of the spinosad tolerances.

Plants: Method GRM 05.04 is a HPLC/MS/MS method which has been determined to be adequate for enforcement of the currently-established spinetoram plant tolerances and was forwarded to FDA (D325387, T. Bloem, 12-SEP-2007; D343662, T. Bloem, 12-SEP-2007). Since method GRM 05.04 has been validated on a wide variety of crops (46695013.der), HED concludes that it is sufficient to enforce the dragon fruit tolerances recommended as part of the current petition. The remaining recommended tolerances reflect an update to the current crop group/subgroup commodity definitions and, therefore, the current enforcement method is also sufficient.

Livestock: Method GRM 05.15 is a HPLC/MS/MS method which has been determined to be adequate for enforcement of the currently-established livestock tolerances and has been forwarded to FDA (D325387, T. Bloem, 12-SEP-2007; D343662, T. Bloem, 12-SEP-2007).

2.2.2 Recommended Tolerances

Table 2.2.2 is a summary of the petitioner-proposed and HED-recommended tolerances for spinosad (combined residues of spinosyns A and D) and spinetoram (combined residues of XDE-175-J, XDE-175-L, ND-J, and NF-J). With the establishment of the tolerances listed in Table 2.2.2, the following spinosad and spinetoram tolerances should be deleted: Brassica, head and stem, subgroup 5A; Brassica, leafy greens, subgroup 5B; vegetable, leafy, except Brassica, group 4 and cranberry.

Table 2.2.2. Tolerance Summary for Spinosad and Spinetoram.

Commodity/ **Correct Commodity Definition**	Proposed New/Revised Tolerance (ppm)	Established Tolerance (ppm)	Recommended Tolerance (ppm)	Comments
Spinosad (40 CFR 180.495(a))				
Dragon fruit	1.5	-	1.5	\
Vegetable, *Brassica*, head and stem, group 5-16	2	-	2	Crop group conversion/revision.
Brassica, head and stem, subgroup 5A	-	2.0	Remove	
Brassica, leafy greens, subgroup 5B	-	10.0	Remove	
Vegetable leafy group 4-16	10	-	10	
Vegetable, leafy, except *Brassica*, group 4	-	8.0	Remove	
Leaf petiole vegetable subgroup 22B	8	-	8	
Berry, low growing, except strawberry, subgroup 13-07H	0.04	-	0.04	
Celtuce	8	-	8	
Fennel, Florence, fresh leaves and stalk	8	-	8	
Kohlrabi	2	-	2	
Cranberry	-	0.01	Remove	Commodity included in Berry, low growing, except strawberry, subgroup 13-07H
Spinetoram (40 CFR 180.635(a))				
Dragon fruit	1.5	-	1.5	\
Vegetable, *Brassica*, head and stem, group 5-16	2	-	2	Crop group conversion/revision.
Brassica, head and stem, subgroup 5A	-	2.0	Remove	
Brassica, leafy greens, subgroup 5B	-	10.0	Remove	
Vegetable leafy group 4-16	10	-	10	
Vegetable, leafy, except *Brassica*, group 4	-	8.0	Remove	

Table 2.2.2. Tolerance Summary for Spinosad and Spinetoram.				
Commodity/ **Correct Commodity Definition**	Proposed New/Revised Tolerance (ppm)	Established Tolerance (ppm)	Recommended Tolerance (ppm)	Comments
Leaf petiole vegetable subgroup 22B	8	-	8	
Berry, low growing, except strawberry, subgroup 13-07H	0.04	-	0.04	
Celtuce	8	-	8	
Fennel, Florence, fresh leaves and stalk	8	-	8	
Kohlrabi	2	-	2	Commodity included in Berry, low growing, except strawberry, subgroup 13-07H
Cranberry	-	0.04	Remove	

2.2.3 Revisions to Petitioned-For Tolerances

No revisions are necessary.

2.2.4 International Harmonization

For *spinosad*, a Codex maximum residue limits (MRL) is not established for dragon fruit; Canadian (0.1 ppm) and Mexican (0.02 ppm) MRLs have been established for dragon fruit. HED concludes that harmonization with the Canadian and Mexican MRLs is not appropriate based on the OECD calculation and the maximum residue from the field trial study on dragon fruit and is recommending for a tolerance value of 1.5 ppm, similar to spinetoram. It is noted that HED previously concluded that based on the similar structures for spinosad and spinetoram and side-by-side spinosad and spinetoram field trail data conducted using selected crops (D325387, T. Bloem, 12-SEP-2007), spinosad residue data may be translate to spinetoram provided the spinetoram application rate is equal to or less than the spinosad rate used in the residue study. Based on this spinetoram in dragon fruit (with maximal use rates being close enough to equal to spinosad), support spinosad tolerances of 1.5 ppm for residues in/on dragon fruit.

Mexico and United States have established MRL at 8 ppm for leaf lettuce, one of the representative crops for Vegetable, leafy, group 4-16; while Codex has it as 10 ppm and Canada as 25 ppm. In this situation, HED recommends harmonization with Codex.

MRLs for Kohlrabi and Vegetable, Brassica, head and stem, group 5-16 are at 2 ppm in Canada, Codex, US, and Mexico. Leaf petiole vegetable subgroup 22B has MRL at 8 ppm in Canada, US, and Mexico while at 2 ppm in Codex. Berry, low growing, except strawberry, subgroup 13-07H has established MRL at 0.01 in US, 1.5 ppm in Mexico and 0.02 ppm in Codex. Celtuce and Fennel, Florence, fresh leaves and stalk do not have Codex MRLs. Celtuce has MRLs of 8 ppm in US, Canada, and Mexico. Fennel, Florence, fresh leaves and stalk has MRLs of 8 ppm in US and Mexico and 0.04 ppm in Canada.

For *spinetoram*, Canadian, Mexican, and Codex MRLs are not established for dragon fruit; therefore, harmonization is not an issue. Vegetable, Brassica, head and stem, group 5-16 has Codex established MRL at 0.3 ppm while US, Mexico and Canada MRLs are at 2 ppm. Vegetable, leafy, group 4-16 has established MRL at 8 pm in the US and Mexico while Canada

MRL is at 30 ppm and Codex at 10 ppm. HED recommends harmonization with Codex. Leaf petiole vegetable subgroup 22B has US/Mexico/Canada MRLs at 8 pm and Codex MRL at 6 ppm. Berry, low growing, except strawberry, subgroup 13-07H has no Codex MRL; US/Canada/Mexico MRLs at 0.04 ppm. Celtuce has no Codex MRL as well while US/Mexico MRL is at 8 ppm and Canada as 0.04 ppm. Fennel, Florence, fresh leaves and stalk has US/Mexico/Canada MRLs at 8 ppm and no Codex MRL. Kohlrabi has MRLs at 2 ppm in Codex and US, 0.04 ppm in Mexico and 0.3 in Canada.

2.3 Label Recommendations

The proposed labels are adequate; no revisions are necessary.

3.0 Introduction

3.1 Chemical Identity

Spinosad, which consists of spinosyn A and spinosyn D (A:D of 85:15), is a fermentation product of *Saccharopolyspora spinosad*. Spinetoram, which consists of XDE-175-J and XDE-175-L (J:L of 3:1), is derived from the synthetic modification of *Saccharopolyspora spinosa* fermentation products. The chemical structure and nomenclature for spinosad and spinetoram are presented in Table 3.1.1 and 3.1.2, respectively.

Table 3.1.1. Spinosad Nomenclature.

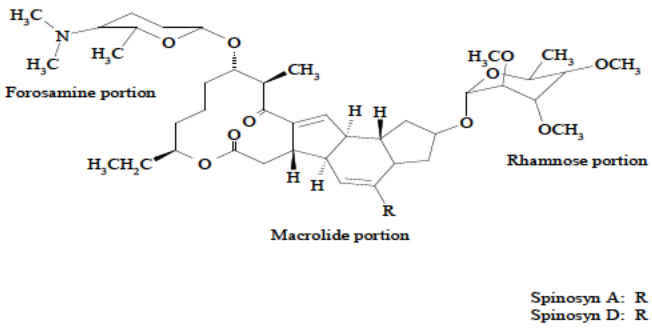
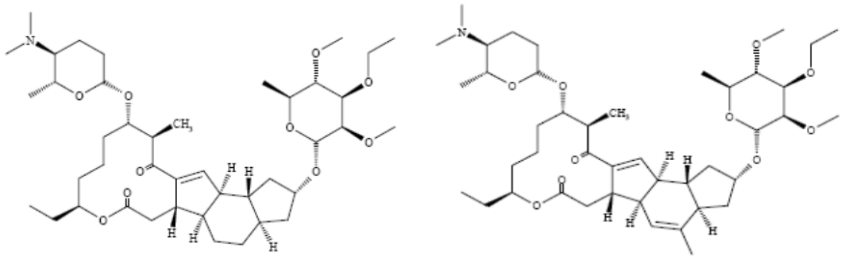
Chemical Structure	
Common name	Spinosad
Company experimental name	XDE-105
IUPAC name	**Spinosyn A:** (2*R*,3a*S*,5a*R*,5b*S*,9*S*,13*S*,14*R*,16a*S*,16b*R*)-2-(6-deoxy-2,3,4-tri-*O*-methyl-α-L-mannopyranosyloxy)-13-(4-dimethylamino-2,3,4,6-tetradeoxy-β-D-erythropyranosyloxy)-9-ethyl-2,3,3a,5a,5b,6,7,9,10,11,12,13,14,15,16a,16b-hexadecahydro-14-methyl-1*H*-8-oxacyclododeca[*b*]*as*-indacene-7,15-dione **Spinosyn D:** (2*S*,3a*R*,5a*S*,5b*S*,9*S*,13*S*,14*R*,16a*S*,16b*R*)-2-(6-deoxy-2,3,4-tri-*O*-methyl-α-L-mannopyranosyloxy)-13-(4-dimethylamino-2,3,4,6-tetradeoxy-β-D-erythropyranosyloxy)-9-ethyl-2,3,3a,5a,5b,6,7,9,10,11,12,13,14,15,16a,16b-hexadecahydro-4,14-dimethyl-1*H*-8-oxacyclododeca[*b*]*as*-indacene-7,15-dione
CAS name	**Spinosyn A:** 2-[(6-deoxy-2,3,4-tri-O-methyl-α-L-manno-pyranosyl)oxy]-13-[[5-(dimethylamino)-tetrahydro-6-methyl-2*H*-pyran-2-yl]oxy]-9-ethyl-2,3,3a,5a,5b,6,9,10,11,12,13,14,16a,16b-tetradecahydro-14-methyl-1*H*-as-Indaceno[3,2-d]oxacyclododecin-7,15-dione **Spinosyn D:** 2-[(6-deoxy-2,3,4-tri-O-methyl-α-L-manno-pyranosyl)oxy]-13-[[5-(dimethylamino)-tetrahydro-6-methyl-2*H*-pyran-2-yl]oxy]-9-ethyl-2,3,3a,5a,5b,6,9,10,11,12,13,14,16a,16b-tetradecahydro-4,14-methyl-1*H*-as-Indaceno[3,2-d]oxacyclododecin-7,15-dione
CAS #	**Spinosyn A:** 131929-60-7; **Spinosyn D:** 131929-63-0

Table 3.1.2. Spinetoram Nomenclature.	
Compound	Chemical Structure  XDE-175-J XDE-175-L
Common name	Spinetoram (mixture of XDE-175-J and XDE-175-L)
Company experimental name	**XDE-175-J:** TSN104472; 3'-O-ethyl 5,6-dihydro spinosyn J; 175-J **XDE-175-L:** TSN104480; 3'-O-ethyl spinosyn L; 175-L
IUPAC name	**XDE-175-J:** (2*R*,3a*R*,5a*R*,5b*S*,9*S*,13*S*,14*R*,16a*S*,16b*R*)-13-{[(2*R*,5*S*,6*R*)-5-(dimethylamino)-6-methyltetrahydro-2*H*-pyran-2-yl]oxy}-9-ethyl-14-methyl-7,15-dioxo-2,3,3a,4,5,5a,5b,6,7,9,10,11,12,13,14,15,16a,16b-octadecahydro-1*H*-as-indaceno[3,2-*d*]oxacyclododecin-2-yl 6-deoxy-3-*O*-ethyl-2,4-di-*O*-methyl-alpha-*L*-mannopyranoside **XDE-175-L:** (2*S*,3a*R*,5a*S*,5b*S*,9*S*,13*S*,14*R*,16a*S*,16b*S*)-13-{[(2*R*,5*S*,6*R*)-5-(dimethylamino)-6-methyltetrahydro-2*H*-pyran-2-yl]oxy}-9-ethyl-4,14-dimethyl-7,15-dioxo-2,3,3a,5a,5b,6,7,9,10,11,12,13,14,15,16a,16b-hexadecahydro-1*H*-as-indaceno[3,2-*d*]oxacyclododecin-2-yl 6-deoxy-3-*O*-ethyl-2,4-di-*O*-methyl-alpha-*L*-mannopyranoside
CAS name	**XDE-175-J:** 1*H*-as-indaceno[3,2-*d*]oxacyclododecin-7,15-dione, 2-[(6-deoxy-3-*O*-ethyl-2,4-di-*O*-methyl-a-*L*-mannopyranosyl)oxy]-13-[[(2*R*,5*S*,6*R*)-5-(dimethylamino)tetrahydro-6-methyl 2*H*-pyran-2-yl]oxy]-9-ethyl-2,3,3a,4,5,5a,5b,6,9,10,11,12,13,14,16a,16b-hexadecahydro 14-methyl-(2*R*,3a*R*,5a*R*,5b*S*,9*S*,13*S*,14*R*,16a*S*,16b*R*) **XDE-175-L:** 1*H*-as-indaceno[3,2-*d*]oxacyclododecin-7,15-dione,2-[(6-deoxy-3-*O*-ethyl-2,4-di-*O*-methyl-a-*L*-mannopyranosyl)oxy]-13-[[(2*R*,5*S*,6*R*)-5-(dimethylamino)tetrahydro-6-methyl-2*H*-pyran-2-yl]oxy]-9-ethyl-2,3,3a,5a,5b,6,9,10,11,12,13,14,16a,16b-tetradecahydro-4,14-dimethyl-(2*S*,3a*R*,5a*S*,5b*S*,9*S*,13*S*,14*R*,16a*S*,16b*S*)
CAS #	**XDE-175-J:** 187166-40-1; **XDE-175-L:** 187166-15-0

3.2 Physical/Chemical Properties

The physical/chemical properties for spinosad and spinetoram are presented in Tables 3.2.1 and 3.2.2 respectively. Spinosad is moderately soluble in water, has a high Log K_{ow}, and is nonvolatile. Spinetoram is weakly soluble in water, has a high log K_{ow}, and is nonvolatile.

Table 3.2.1. Spinosad Physicochemical Properties.	
Melting range	Spinosyn A: 84-99.5°C; Spinosyn D: 161.5-170°C
pH (10% slurry of spinosad in water)	7.74
Density	0.512 g/ml (20°C)
Water solubility (ppm; distilled water)	Spinosyn A: 89.4 ppm; Spinosyn D: 0.495 ppm
Vapor pressure (kPa; 25°C)	Spinosyn A: 3.0×10^{-11}; Spinosyn D: 2.0×10^{-11}
Dissociation constant (pK_a)	not available
Octanol/water partition coefficient Log (K_{OW})	Spinosyn A: 2.8 (pH 5), 4.0 (pH 7), and 5.2 (pH 9) Spinosyn D: 3.2 (pH 5), 4.5 (pH 7), and 5.2 (pH 9)
UV/visible absorption spectrum	not available

Table 3.2.2. Spinetoram Physicochemical Properties.	
Melting points	XDE-175-J: 143.4°C; XDE-175-L: 70.8°C
pH	6.46 (1% w/w aqueous solution)
Density	1.1485 g/ml (20°C)
Water solubility (purified water; pm; 20°C)	XDE-175-J: 10.0 ppm; XDE-175-L 31.9 ppm
Vapor pressure (Pa; 25°C)	XDE-175-J: 5.3×10^{-5}; XDE-175-L: 2.1×10^{-5}
Dissociation constant (pKa)	XDE-175-J: pKa = 7.86; XDE-175-L: pKa = 7.59
Octanol/water partition coefficient Log K_{ow} (20°C)	XDE-175-J: 2.44 (pH 5), 4.09 (pH 7), 4.22 (pH 9) XDE-175-L: 2.94 (pH 5), 4.49 (pH 7), 4.82 (pH 9)
UV/visible absorption spectrum	XDE-175-J: 245 nm (λmax; 12200 ε, L/(mol*cm) extinction coefficient) XDE-175-L: 243 nm (λmax; 11100ε, L/(mol*cm) extinction coefficient)

3.3 Pesticide Use Pattern/Directions

Table 3.3.1 is a summary of the proposed use patterns. The petition submitted by the registrant includes the aforementioned crop group conversion/expansions as well as the addition of dragon fruit (pitaya) to the Radiant® SC (spinetoram; EPA Reg.# 62719-545), Delegate® WG Insecticide (spinetoram; EPA Reg.# 62719-541), and Entrust® SC (spinosad; EPA Reg.# 62719-671) product labels. Table 3.3.1 is a summary of the end-use products and target pests and Table 3.3.2 is a summary of the proposed application scenarios.

HED concludes that the proposed application scenarios are supported by the available residue chemistry data.

Table 3.3.1. Summary of End-Use Products.					
Trade Name	Conc.	Formulation	Label Date	Target Crops	Target Pests
Spinetoram					
Delegate® WG (EPA Reg. No. 62719-541)	25%	water-dispersible granule	not specified	Dragon fruit; Vegetable, *Brassica*, head and stem, group 5-16; Kohlrabi; Vegetable, leafy group 4-16; Leaf petiole vegetable subgroup 22B; Celtuce; Fennel, Florence, fresh leaves and stalk; Berry, low growing, except strawberry, subgroup 13-07H	For control or suppression of lepidopterous larvae (worms, caterpillars), dipterous leafminers, thrips, and certain psyllids in asparagus, banana and plantain, Brassica cole crops, bulb vegetables, bushberries, caneberries, cereal grains (except rice, millet and sorghum), citrus, coffee, corn (field, sweet, popcorn, and seed corn), cotton, cranberry, cucurbits, dates, fig, fruiting vegetables (tomato, peppers, and eggplant), globe artichoke, grain amaranth, grape, herbs, hops, leafy vegetables, leaves of legume vegetables, leaves of root and tuber vegetables, legume vegetables (succulent and dried beans and peas), okra, peanut, peppermint, pineapple, pistachios, pome fruits, pomegranate, quinoa, root and tuber
Radiant® SC (EPA Reg. No. 62719-545)	1 lb ai/gallon	soluble concentrate	not specified		

Table 3.3.1. Summary of End-Use Products.					
Trade Name	Conc.	Formulation	Label Date	Target Crops	Target Pests
					vegetables, root vegetables, soybean, spearmint, spices (except black pepper), stone fruits, strawberry, teosinte, tree nuts, tropical tree fruits, turnip greens and watercress.

Table 3.3.2. Summary of Directions of Use for Spinetoram.						
Applic. Timing, Type, and Equip.	Formulation [EPA Reg. No.]	Applic. Rate (lb ai/A)	Max. No. Applic. per Season	Max. Seasonal Applic. Rate (lb ai/A)	PHI (days)	Use Directions and Limitations
Dragon Fruit						
Foliar Ground, aerial	Spinetoram Delegate® WG [62719-541]	0.062-0.109	4	0.375	1	Min. RTI = 4 days Min spray volume = 5 GPA (ground), 10 GPA (air) REI = 4 hours
	Spinetoram Radiant® SC [62719-545]	0.063-0.109				

PHI = preharvest interval; RTI = retreatment interval.

4.0 Metabolism/Degradate Residue Profile

Nature of the Residue

Spinosad: The following text and Table 4.0.1 are summaries of the spinosad residues of concern in primary crops, rotational crops, livestock, and fish.

Primary Crops: The qualitative nature of the residue in plants is adequately understood based on metabolism studies conducted on cotton, apple, cabbage, tomato, and turnip (D228434, S. Willett, 23-JAN-1997; foliar application). Spinosyns A and D, were the major residues identified in early-harvest samples (preharvest interval (PHI) = 0-3 days); minor metabolites identified include spinosyn B (*N*-demethyl spinosyn A), *N*-demethyl spinosyn D, spinosyn K (*O*-demethyl spinosyn A), and *N*-formyl spinosyn B. In samples collected at subsequent intervals, the residue levels of spinosyns A and D declined significantly accompanied by incremental increases in nonextractable and polar residues. Extensive fractionation and characterization of nonextractable and polar residues in selected raw agricultural commodities (RAC) samples indicates that most of the radioactivity was degraded to multicomponent residues of low molecular weight which are subsequently incorporated into natural plant constituents.

The primary crop metabolism studies demonstrated a rapid dissipation of spinosyns A and D with evidence that photolysis plays a role in initial degradation. The proposed metabolic pathway involves the N- and/or O-demethylation of spinosyns A and D followed by further modification to form polar and nonextractable residues. The HED MARC discussed these data and determined that the residues of concern in plants for tolerance enforcement and risk assessment purposes are spinosyns A and D (D243816, G. Herndon, 03-MAR-1998).

Livestock: The nature of the residue in livestock is adequately understood based on metabolism studies conducted on ruminants (oral and dermal), and poultry (oral). The metabolic pathway involved either the loss of a single methyl group from the N-methyl moiety on the forosamine sugar and/or the hydroxylation of the macrolide at several different positions. HED concluded that the residue of concern in livestock for risk assessment and tolerance enforcement purposes are spinosyns A and D (D243816, G. Herndon, 03-MAR-1998; D264984, W. Donovan, 14-JUN-2002).

Subsequent to this decision, the petitioner requested dermal application to poultry. Generally, HED requires a dermal metabolism study to support dermal application but waived this requirement for spinosad for the following reasons (D374794, T. Bloem, 25-MAR-2010): (1) the poultry oral metabolism study which involved exposure of spinosad to the digestive system and a first pass through the liver resulted in only parent as a residue of concern; (2) the poultry dermal magnitude of the residue study quantified the major residues identified in the poultry oral metabolism study (parent and N- and O-demethyl spinosyns A and D); and (3) spinosad has low toxicity with the most recent human health risk assessment yielding exposures less than HED's level of concern while assuming 100% crop treated for food commodities (D376415, T. Bloem, 12-OCT-2010). Based on the above considerations and the results of the poultry dermal magnitude of the residue study, HED concluded that the residues of concern in poultry following dermal exposure for tolerance enforcement and risk assessment purposes in all commodities excluding liver are spinosyns A and D (parent); the residues of concern in poultry liver following dermal exposure for purposes of tolerance enforcement are spinosyns A and D (parent) and for risk assessment are spinosyns A, B, D, J, N-demethyl D, and N-demethyl J.

Rotational Crops: Based on the results of a confined rotational crop study, the MARC concluded that the residues of concern in rotational crops are spinosyn A and D (D243816, G. Herndon, 03-MAR-1998; field rotational crop data have not been submitted). The confined study was conducted at 0.98 lb ai/acre (2.0x) and employed wheat, lettuce, and radish at PBIs of 30, 120, and 365 days. The data indicated that spinosad was metabolized to the point where it entered the general carbon pool (residues of spinosyns A and D were not detected). It did not appear that the parent compound was taken up and/or translocated within the rotational crops tested. Field rotational crop data have not been submitted and are not required.

Fish/shellfish: Spinosad is currently registered for direct application to water as a mosquito larvicide and residues in/on fish/shellfish may occur. Based on the results of a fish bioaccumulation study, HED concluded that the residues of concern in fish/shellfish for tolerance enforcement are spinosyn A and D (D316078, T. Bloem, 2-AUG-2006). For purposes of risk assessment, HED concluded that adjustment of the TRRs in the edible tissues from the 19 ppb spinosyn A bioconcentration study for the EFED water concentration resulting from the mosquito larvicide use is acceptable for the following reasons (fish/shellfish residue study is unnecessary): (1) spinosyn A is the major residue in spinosad (spinosyn A:spinosyn D = 85:15); (2) the fish bioconcentration study indicated that the metabolic pathway in fish proceeds via demethylation of the forosamine ring which is similar to the metabolic pathway observed in apple, cabbage, cotton, tomato, turnip, ruminants (oral and dermal), and poultry (oral); based on this similar metabolic pathway, HED does not anticipate the presence of metabolites in fish/shellfish which are more toxic than parent; (3) the bioconcentration study demonstrated

rapid clearance of TRRs when the fish were moved to untreated water; (4) the bioconcentration study employed a sufficient dosing interval (28 days); (5) the water concentration provided by EFED for the mosquito larvicide use is conservative as it assumes that the entire water body is treated and static conditions (no inflow, outflow, or dilution); and (6) low toxicity for spinosad (no acute or cancer assessments required).

Table 4.0.1. Residues for Tolerance Expression and Risk Assessment for Spinosad.

Matrix	Residues included in Risk Assessment	Residues included in Tolerance Expression
Plants[1]	spinosyn A and D	spinosyn A and D
Hog and Ruminants[1]	oral and dermal - spinosyn A and D	oral and dermal - spinosyn A and D
Poultry[1,2]	oral - spinosyn A and D; dermal (excluding liver) - spinosyn A and D; dermal (liver) - spinosyns A, B, D, J, *N*-demethyl D, and *N*-demethyl J	oral and dermal spinosyn A and D
Rotational Crops[1]	spinosyn A and D	spinosyn A and D
Drinking Water[3]	total spinosad	--
Fish/Shellfish[4]	adjustment of the TRRs in the edible tissues from the spinosyn A bioconcentration study (19 ppb data) for the EFED water concentration resulting from the mosquito larvicide use	spinosyn A and D

[1] D243816, G. Herndon, 03-MAR-1998; D264984, W. Donovan, 14-Jun-2002.
[2] D374794, T. Bloem, 25-MAR-2010.
[3] D316077, T. Bloem *et al.*, 02-AUG-2006.
[4] HED notes that these conclusions are appropriate for this mosquito larvicide petition only and will be reevaluated if the petitioner alters the aquatic application scenario (D316077, T. Bloem *et al.*, 02-Aug-2006).

Spinetoram: The following text and Table 4.0.2 are summaries of the residues of concern in primary crops, rotational crops, and livestock. Based on the available data and since spinetoram is not registered for direct application to water, resides in fish are expected to be negligible.

Primary Crops: The petitioner submitted turnip, apple, and lettuce metabolism studies conducted with spinetoram (XDE-175-J and XDE-175-L) uniformly labeled throughout the macrolide ring (4.0-9.0x the proposed rate; foliar application). Based on these data, it appears that three metabolic pathways are responsible for the breakdown of spinetoram in plants. One pathway involves changes to the N-demethyl moiety on the forosamine sugar to give the N-demethyl (<1-20% TRR) and N-formyl (<1-17% TRR) metabolites. Due to the presence of these metabolites in the 0-day PHI samples, it is thought that these changes may be the result primarily of photolysis. The second pathway involves cleavage of the macrolide ring system at one or more positions, ultimately resulting in a complex residue mixture consisting of numerous components (≤89% TRR). The third pathway involves changes to the rhamnose sugar of XDE-175-J only, producing the 3-O-deethyl (≤4% TRR) and C9-pseudoaglycone metabolites (; ≤4% TRR) or cleavage of the forosamine sugar to yield C17-pseudoaglycone-175-J (turnip tops only; <1% TRR). All of the forosamine-altered metabolites and rhamnose-altered metabolites were subject to breakdown via the second pathway and, therefore, the second pathway ultimately predominated in the residue profile for both test materials. It is presumed that XDE-175-L also underwent degradation by the third pathway, but was degraded too quickly via the second pathway to enable detection of any metabolites. Based on the turnip, apple, and lettuce metabolism studies, HED concludes that the residues of concern in plants are as summarized in Table 4.0.2. For further information concerning these conclusions, see the HED human health risk assessment D331741 (PV Shah *et al.*, 20-Sep-2007).

Livestock: The petitioner submitted goat and hen metabolism studies conducted with spinetoram

(XDE-175-J and XDE-175-L) uniformly labeled throughout the macrolide ring (dietary burden of 10 ppm). No significant metabolism of spinetoram was observed in ruminants as the unchanged parent molecule was the primary residue component identified in milk and all tissue samples (26-84% TRR). Ruminant liver and muscle contained one unidentified metabolite (XDE-175-J - <10% TRR; XDE-175-L - <27% TRR); ruminant liver also contained a minor amount of ND-J and ND-L (≤2% TRR). Parent was also the primary residue component in all hen matrices (45-80% TRR) excluding liver (12-13% TRR). In hen liver, the O-deethyl (≤18% TRR) and O-demethyl (≤20% TRR) metabolites were also observed indicating that the metabolic pathway in hens is primarily through dealkylation of the rhamnose sugar. Based on the goat and hen metabolism studies, HED concludes that the residues of concern in livestock are as summarized in Table 4.0.2. For further information concerning these conclusions, see the HED human health risk assessment D331741 (PV Shah *et al.*, 20-SEP-2007).

Rotational Crops: The petitioner submitted a confined rotational crop study conducted with spinetoram (XDE-175-J or XDE-175-L) uniformly labeled throughout the macrolide ring (46695021.der.doc; 47396301.der.doc). Lettuce, radish, and wheat were planted 30, 120, and 365 days after a single application of XDE-175-J or XDE-175-L at 0.36 lb ai/acre or 0.12 lb ai/acre, respectively. TRRs were ≤0.045 ppm in/on all harvested commodities. Adequate residue identification/characterization procedures were performed which resulted in the identification of XDE-175-J and ND-J, NF-J, and/or O-desethyl-175-J (HPLC method did not distinguish these three compounds) in radish tops (immature) and lettuce (immature and mature) collected from the XDE-175-J treated plot at 16-29% TRR (0.007-0.025 ppm; <0.01 ppm in the mature crops). Although HED identified some issues with the sample work-up procedure, the study did demonstrate that TRRs in rotational crops were low following a single soil application at a combined rate of 0.45 lbs spinetoram/acre and that qualitatively, residues in rotational crops are not likely to be more toxic than parent. Based on the confined rotational crop study, a determination of the residues of concern in rotational could not be made (field rotational crop study has not been submitted). However, based on these data and since the proposed seasonal application rate is <0.45 lb ai/acre, HED concludes that a 30-day PBI is appropriate for all nonlabeled crops.

Table 4.0.2. Residues for Tolerance Expression and Drinking Water Risk Assessment for Spinetoram.

Matrix	Residues Included in Drinking Water Risk Assessment	Residues Included in Tolerance Expression
Plants	XDE-175-J, XDE-175-L, ND-J, and NF-J	XDE-175-J, XDE-175-L, ND-J, and NF-J
Rotational Crops	Not determined. Based on the available data and provided the application rate is ≤0.45 lb ai/acre, the following rotational crop restrictions are appropriate: labeled crops may be rotated immediately to a treated field and nonlabeled crops may be rotated 30 days after application.	
Ruminants[1]	XDE-175-J, XDE-175-L, ND-J, and NF-J	XDE-175-J, XDE-175-L, ND-J, and NF-J
Hen[1]	XDE-175-J, XDE-175-L, ND-J, NF-J, 3'-O-deethyl-175-J, 3'-O-deethyl-175-L, and O-demethyl-175-L[2]	XDE-175-J, XDE-175-L, ND-J, and NF-J

[1] ND-J and NF-J were included as residues of concern in livestock due to their presence in/on feed commodities.
[2] O-demethyl-175-L is either 2'-O-demethyl-175-L or 4'-O-demethyl-175-L or a mixture of both.

4.1 Comparison of Metabolic Pathways

Spinosad: The metabolic pathway in crops (primary and rotational), livestock, fish, and rat were similar and involved demethylation of the forosamine ring, demethylation of the rhamnose ring, and/or hydroxylation of the macrolide. In primary crops, spinosad was further degraded to

multiple low molecular weight compounds which are subsequently incorporated into natural plant constituents.

Spinetoram: The metabolic pathway in crops, livestock, and rats were qualitatively similar. The metabolic pathway in primary crops involved demethylation of the forosamine ring, changes to the rhamnose ring producing the 3-*O*-deethyl, and/or cleavage of the rhamnose ring. Parent and the metabolites were ultimately subjected to opening of the macrolide ring system at several positions resulting in numerous components with this pathway predominating in the residue profile. The confined rotation crop study resulted in a similar metabolic profile as primary crops (soil application at 0.45 lb ai/acre). No significant metabolism of spinetoram was observed in ruminants as the unchanged parent molecule was the primary residue component identified in milk and tissue samples. Ruminant liver and muscle contained one unidentified metabolite (XDE-175-J - <10% TRR; XDE-175-L - <27% TRR) and minor amounts of ND-J and ND-L. In hen, parent was the major residue in egg and all tissues except liver where parent and the demethylated and/or deethylated metabolites predominated. In the rat, the major route of metabolism was found to be glutathione conjugation with the parent compound, as well as glutathione conjugation with *N*-demethylated, *O*-deethylated, and hydroxylated forms of parent.

5.0 Residue Profile

5.1 Residue Analytical Methods

5.1.1 Data Collection Methods

50854301.der

A spinetoram magnitude of the residue study was submitted in support of the proposed application of spinosad and spinetoram to dragon fruit (MRID 50854301). The method was adequately validated. The paragraph below is a brief description of the method.

MRID 50854301 (dragon fruit)- Samples were analyzed for residues of spinetoram, determined as XDE 175 J and XDE 175 L, and metabolites ND J, and NF J, using a method based on Dow AgroSciences Methods GRM 05.03 and GRM 05.04, high-performance liquid chromatography methods with tandem mass spectrometry detection (LC/MS/MS). Residues of all analytes (XDE 175 J, XDE 175 L, ND J, and NF J) were converted to spinetoram equivalents (a 3:1 mixture of XDE 175 J and XDE 175 L) by the study reviewer using molecular weight conversion factors (MWCFs) of 1.004 for XDE 175 J, 0.988 for XDE 175 L, 1.023 for ND J, and 0.986 for NF J. The limit of quantitation (LOQ; determined as the lowest level of method validation, LLMV) was 0.010 ppm for each analyte, and the combined LOQ was 0.040 ppm. Acceptable method validation and concurrent recoveries were obtained from samples of dragon fruit fortified with a mixed standard solution of XDE 175 J, XDE 175 L, ND J, and NF J, each at 0.010-1.0 ppm. The fortification levels adequately represented measured residue levels.

5.1.2 Food and Drug Administration (FDA) Multiresidue Methods (MRMs)

Spinosad: Data pertaining to FDA MRMs testing of spinosyns A, D, B, K, and N-demethyl-D were submitted and demonstrate that these compounds are not quantifiable using the describe procedures; these data were forwarded to FDA (D228434, S. Willett, 23-JAN-1997; G. Herndon, 1-MAY-1996).

Spinetoram: Data pertaining to the FDA MRMs testing of XDE-175-J, XDE-175-L, ND-J, NF-J, ND-L, and NF-L were submitted. None of the test substances were found to be fluorescent using procedures outlined in Protocol A. All test substances were subjected to Protocol C, modules DG1, DG5, DG13, DG17 and DG18. Test substances were determined to be non-chromatographable by the chosen gas chromatography modules described in Protocol C. Due to the poor sensitivity of the test substances to detection by methods described in Protocol C, no further analyses were performed by Protocols D, E or F. Since the test substances are not acids, phenols, or substituted ureas, analyses were not performed using Protocols B or G. These data were forwarded to the FDA (D335229, T. Bloem, 18-JAN-2007).

5.1.3 Tolerance-Enforcement Methods

See Section 2.2.1

5.1.4. Submittal of Analytical Reference Standards (860.1650)

Analytical standards of spinetoram/spinosad are currently available in the National Pesticide Standards Repository [source: personal communication with T. Cole of Analytical Chemistry Laboratory, April 23, 2020].

5.2 Storage Stability

A summary of the sample storage conditions and durations for the spinetoram dragon fruit samples submitted in support of the current petitions are summarized in Table 5.2.1. To support sample storage durations, a concurrent storage stability study was conducted using untreated samples of dragon fruit from Trial FL167 fortified with a mixed standard solution of XDE-175-J, XDE-175-L, ND-J, and NF-J at 0.1 ppm each; no 0-day data were provided. These data demonstrate that residues of XDE-175-J, XDE-175-L, ND-J, and NF-J are stable during frozen storage in dragon fruit for at least 11.2 months. These data are acceptable to support the storage conditions and durations of the samples from the submitted field trials.

Table 5.2.1. Summary of Storage Conditions.

Matrix	Storage Temperature (°C)	Actual Storage Duration[1]	Interval of Demonstrated Storage Stability
Dragon fruit	<0	114-318 days (3.7-10.4 months)	Residues of XDE-175-J, XDE-175-L, ND-J, and NF-J are stable in dragon fruit during frozen storage for at least 11.2 months.[2]

[1] Interval from harvest to extraction. Samples were analyzed within 0-4 days of extraction.
[2] Concurrent storage stability study.

HED concludes that these data, combined with previously submitted storage stability data, are sufficient to validate the current study:

5.3 Residue Data

5.3.1 Crop Field Trials

50854301.der

Based on spinosad and spinetoram side-by-side field trail data which indicated residues were similar provided the application rate was similar and since spinetoram application rates are generally equal to or lower than that for spinosad, HED concluded that the spinosad residue data may translated to spinetoram. (D325387, T. Bloem, 12-SEP-2007).

Spinetoram dragon fruit trials were conducted at the proposed rate that would be 85% of the spinosad rate and HED concludes that this is close enough therefore, the spinetoram data may be translated to spinosad.

Crop Group Updates: The remaining proposed tolerances pertain to updates to the crop group/subgroup commodity definitions. Since the proposed application scenarios are identical to that previously reviewed, no residue data were submitted, and none are required. HED concludes that the proposals are adequate.

Table 5.3.1. Summary of Residues from Dragon Fruit Field Trials with Spinetoram.

Crop Matrix	Analyte	Total Application Rate (lb ai/A)	PHI (days)	n[1]	Residues (ppm spinetoram equivalents)						
					Min.[2]	Max.[2]	LAFT[3]	HAFT[3]	Median[3]	Mean[3]	SD[3]
Dragon fruit	XDE-175-J	0.381-0.395	3	4	0.014	0.162	0.015	0.161	0.033	0.061	0.068
	XDE-175-L			4	<0.010	0.043	<0.010	0.043	0.012	0.019	0.016
	ND-J			4	<0.010	0.101	<0.010	0.095	0.016	0.034	0.040
	NF-J			4	0.026	0.368	0.026	0.341	0.044	0.114	0.152
	Combined[4]			4	<0.085	0.673	0.087	0.640	0.093	0.228	0.274

[1] n = number of independent field trials.
[2] Values based on residues in individual samples.
[3] Values based on per-trial averages. LAFT = lowest average field trial, HAFT = highest average field trial, SD = standard deviation. For computation of the LAFT, HAFT, median, mean, and standard deviation, values <LOQ are assumed to be at the LOQ (0.010 ppm for each analyte).
[4] Combined residues of XDE-175-J, XDE-175-L, ND-J, and NF-J.

5.3.2 Field Rotational Crops

Spinosad: Based on the results of a confined rotational crop study, the MARC concluded that the residues of concern in rotational crops are spinosyn A and D (D243816, G. Herndon, 03-MAR-1998). The confined study was conducted at 0.98 lb ai/acre (2.0x) and employed wheat, lettuce, and radish at PBIs of 30, 120, and 365 days. The data indicated that spinosad was metabolized to the point where it entered the general carbon pool (residues of spinosyns A and D were not detected). It did not appear that the parent compound was taken up and/or translocated within the rotational crops tested. Based on these data and previous conclusions, rotational crops restrictions/tolerances are not required for the currently-proposed crops. Field rotational crop data have not been submitted and are not required.

Spinetoram: The petitioner submitted a confined rotational crop study conducted with XDE-175-J or XDE-175-L each uniformly labeled throughout the macrolide ring (46695021.der.doc; 47396301.der.doc). Lettuce, radish, and wheat were planted 30, 120, and 365 days after a single

application of XDE-175-J or XDE-175-L at 0.36 lb ai/acre or 0.12 lb ai/acre, respectively. TRRs were ≤0.045 ppm in/on all harvested commodities. Adequate residue identification/characterization procedures were performed which resulted in the identification of XDE-175-J and ND-J, NF-J and/or O-desethyl-175-J (HPLC method did not distinguish these three compounds) in radish tops (immature) and lettuce (immature and mature) collected from the XDE-175-J treated plot at 16-29% TRR (0.007-0.025 ppm; <0.01 ppm in the mature crops). Although HED identified some issues with the sample work-up procedure, the study did demonstrate that TRRs in rotational crops were low following a single soil application at a combined rate of 0.36 lbs spinetoram/acre and that qualitatively, residues in rotational crops are not likely to be more toxic than parent. Based on the confined rotational crop study, a determination of the residues of concern in rotational could not be made (field rotational crop study has not been submitted). However, based on these data and since the proposed seasonal application rate is <0.45 lb ai/acre, HED concludes that a 30-day PBI is appropriate for all nonlabeled crops. A field rotational crop study has not been submitted and is unnecessary.

5.3.3 Processed Food/Feed

No processed commodity is associated with this petition.

5.4 Food Residue Profile

Spinosad and spinetoram are registered for application to numerous food/feed crops; spinosad is also registered for application as a mosquito larvicide and for application to livestock premises. As a result of these uses, dietary (food and water) exposure to spinosad and spinetoram is possible including exposure to spinosad residues in fish/shellfish as a result of the mosquito larvicide use.

6.0 Tolerance Derivation

Table 2.2.2 is a summary of the petitioner proposed and HED recommended tolerances for spinosad (combined residues of spinosyns A and D) and spinetoram (combined residues of XDE-175-J, XDE-175-L, ND-J, and NF-J). The dragon fruit (pitaya) tolerance was based on four field trials conducted in NAFTA Growing Zone 13 (FL and HI). The residue data for spinetoram were entered into the Organization for Economic Co-operation and Development (OECD) MRL calculator. The recommended tolerance for the combined residues of spinetoram is 1.5 ppm in/on dragon fruit. Adequate field trial data have been previously submitted for the proposed crop/subgroup conversions.

For *spinetoram*, Canadian, Mexican and Codex MRLs are not established for dragon fruit; therefore, harmonization is not an issue. For *spinosad*, Codex MRL is not established; Canadian (0.1 ppm) and Mexican (0.02 ppm) MRLs have been established. HED concludes that harmonization with the Canadian and Mexican MRLs is not appropriate as the maximum residue from the field trial study on dragon fruit and is recommending for a tolerance of 1.5 ppm similar to spinetoram. It is noted that HED previously concluded that based on the similar structures for spinosad and spinetoram and side-by-side spinosad and spinetoram field trail data conducted using selected crops (D325387, T. Bloem, 12-SEP-2007), spinosad residue data may be translate to spinetoram provided the spinetoram application rate, as is the case here, is equal to or less than

the spinosad rate used in the residue study Spinetoram dragon fruit trials were conducted at the proposed rate that would be 85% of the spinosad rate and HED concludes that this is close enough therefore, the spinetoram data may be translated to spinosad.

Attachment 1: International Residue Limits.
Attachment 2: Chemical Names and Structures.
Attachment 3: Tolerance Calculations (OECD).

Attachment 1: International Residue Limits.

Spinosad: Summary of US and International Tolerances and Maximum Residue Limits

Residue Definition			
US	Canada	Mexico[2]	Codex[3]
Spinosad (180.495): Spinosyn A (Factor A: CAS # 131929-60-7; 2-[(6-deoxy-2,3,4-tri-O -methyl-α-L-manno-pyranosyl)oxy]-13-[[5-(dimethylamino)-tetrahydro-6-methyl-2H-pyran-2-yl]oxy]-9-ethyl-2,3,3a,5a,5b,6,9,10,11,12,13,14,16a,16b-tetradecahydro-14-methyl-1H-as-Indaceno[3,2-d]oxacyclododecin-7,15-dione; and Spinosyn D (Factor D; CAS # 131929-63-0; 2-[(6-deoxy-2,3,4-tri-O-methyl-α-L-manno-pyranosyl)oxy]-13-[[5-(dimethyl-amino)-tetrahydro-6-methyl-2H-pyran-2-yl]oxy]-9-ethyl-2,3,3a,5a,5b,6,9,10,11,12,13,14,16a,16b-tetradecahydro-4,14-methyl-1H-as-Indaceno[3,2-d]oxacyclododecin-7,15-dione.	Spinosyn A and Spinosyn D:	--	spinosyn A and spinosyn D

Tolerance/Maximum Residue Limit (ppm)				
Commodity[1]	US	Canada	Mexico	Codex
Dragon Fruit	1.5	0.1	0.02	--
Vegetable, leafy, group 4-16	10	25	8	10
Vegetable, *Brassica*, head and stem, group 5-16	2	2	2	2
Leaf petiole vegetable subgroup 22B	8	8	8	2
Berry, low growing, except strawberry, subgroup 13-07H	0.04	0.04	1.5	0.04
Celtuce	8	8	8	-
Fennel, Florence, fresh leaves and stalk	8	0.04	8	-
Kohlrabi	2	2	2	2

Spinetoram: Summary of US and International Tolerances and Maximum Residue Limits

Residue Definition			
US	Canada	Mexico	Codex
Spinetoram (180.635): XDE-175-J (1-H-as-indaceno[3,2-d]oxacyclododecin-7,15-dione, 2-[(6-deoxy-3-O-ethyl-2,4-di-O-methyl-a-L-mannopyranosyl) oxy]-13-[[(2R,5S,6R)-5- (dimethylamino)tetrahydro-6-methyl-2H-pyran-2-yl] oxy]-9-ethyl-2,3,3a,4,5,5a,5b,6,9, 10,11,12,13,14,16a,16b- hexadecahydro 14-methyl-, (2R,3aR,5aR,5bS,9S, 13S,14R,16aS,16bR); XDE-175-L: 1H-as-indaceno[3,2-d]oxacyclododecin-7,15-dione, 2-[(6-deoxy-3-O- ethyl-2,4-di-O-methyl-a-L-mannopyranosyl)oxy]-13-[[(2R,5S,6R)-5-(dimethylamino)tetrahydro-6-methyl-2H-pyran-2-yl]oxy]-9-ethyl-2,3,3a,5a,5b,6,9, 10,11,12,13,14,16a,16b-tetradecahydro-4,14-dimethyl-, (2S,3aR,5aS,5bS,9S, 13S,14R,16aS,16bS); ND-J ((2R,3aR,5aR,5bS,9S, 13S,14R,16aS,16bR)-9-ethyl-14-methyl-13-[[(2S,5S,6R)-6-methyl-5-(methylamino)tetrahydro- 2H-pyran-2-yl]oxy]-7,15-dioxo-2,3,3a,4,5,5a,5b,6,7,9, 10,11,12,13,14,15,16a,16b- octadecahydro-1H-as-indaceno[3,2-d]oxacyclododecin-2-yl 6-deoxy-3-O-ethyl-2,4-di-O-methyl- alpha-L-mannopyranoside); and NF-J ((2R,3S,6S)-6-([(2R,3aR,5aR,5bS,9S, 13S,14R,16aS,16bR)- 2-[(6-deoxy-3-O-ethyl-2,4-di-O- methyl-alpha-L-mannopyranosyl) oxy]-9-ethyl-14-methyl-7,15-dioxo-2, 3,3a,4,5,5a,5b,6,7,9, 10,11,12,13,14,15,16a,16b- octadecahydro-1H-as- indaceno[3,2-d]oxacyclododecin-13-yl] oxy)-2-methyltetrahydro- 2H-pyran-3-yl(methyl)formamide)	XDE-175-J, XDE-175-L, N-demethyl-175-J (ND-J), and N-formyl-175-J (NF-J)	--	Spinetoram

Tolerance/Maximum Residue Limit (ppm)				
Commodity[1]	US	Canada	Mexico	Codex
Dragon Fruit	1.5	--	--	--
Vegetable, *Brassica*, head and stem, group 5-16	2.0	2	2	0.3
Vegetable, leafy, group 4-16	10	30	8	10
Leaf petiole vegetable subgroup 22B	8	8	8	6
Berry, low growing, except	0.04	0.04	0.04	-

Spinetoram: Summary of US and International Tolerances and Maximum Residue Limits

Residue Definition

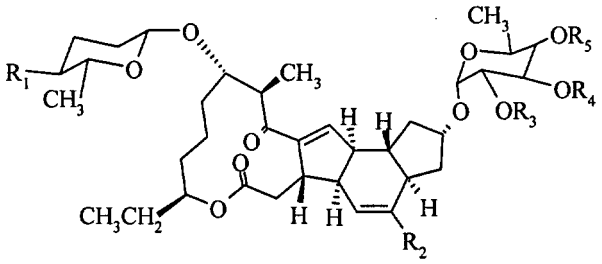
US	Canada	Mexico	Codex
Spinetoram (180.635): XDE-175-J (1-H-as-indaceno[3,2-d]oxacyclododecin-7,15-dione, 2-[(6-deoxy-3-O-ethyl-2,4-di-O-methyl-a-L-mannopyranosyl) oxy]-13-[[(2R,5S,6R)-5- (dimethylamino)tetrahydro-6-methyl-2H-pyran-2-yl] oxy]-9-ethyl-2,3,3a,4,5,5a,5b,6,9, 10,11,12,13,14,16a,16b- hexadecahydro 14-methyl-, (2R,3aR,5aR,5bS,9S, 13S,14R,16aS,16bR); XDE-175-L: 1H-as-indaceno[3,2-d]oxacyclododecin-7,15-dione, 2-[(6-deoxy-3-O- ethyl-2,4-di-O-methyl-a-L-mannopyranosyl)oxy]-13-[[(2R,5S,6R)-5-(dimethylamino)tetrahydro-6-methyl-2H-pyran-2-yl]oxy]-9-ethyl-2,3,3a,5a,5b,6,9, 10,11,12,13,14,16a,16b-tetradecahydro-4,14-dimethyl-, (2S,3aR,5aS,5bS,9S, 13S,14R,16aS,16bS); ND-J ((2R,3aR,5aR,5bS,9S, 13S,14R,16aS,16bR)-9-ethyl-14-methyl-13-[[(2S,5S,6R)-6-methyl-5-(methylamino)tetrahydro- 2H-pyran-2-yl]oxy]-7,15-dioxo-2,3,3a,4,5,5a,5b,6,7,9, 10,11,12,13,14,15,16a,16b- octadecahydro-1H-as-indaceno[3,2-d]oxacyclododecin-2-yl 6-deoxy-3-O-ethyl-2,4-di-O-methyl- alpha-L-mannopyranoside); and NF-J ((2R,3S,6S)-6-([(2R,3aR,5aR,5bS,9S, 13S,14R,16aS,16bR)- 2-[(6-deoxy-3-O-ethyl-2,4-di-O- methyl-alpha-L-mannopyranosyl) oxy]-9-ethyl-14-methyl-7,15-dioxo-2, 3,3a,4,5,5a,5b,6,7,9, 10,11,12,13,14,15,16a,16b- octadecahydro-1H-as- indaceno[3,2-d]oxacyclododecin-13-yl] oxy)-2-methyltetrahydro- 2H-pyran-3-yl(methyl)formamide)	XDE-175-J, XDE-175-L, N-demethyl-175-J (ND-J), and N-formyl-175-J (NF-J)	--	Spinetoram

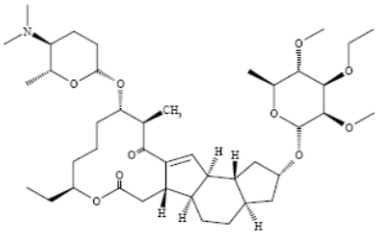
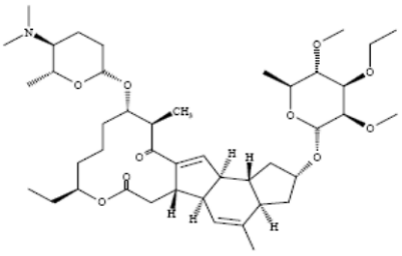
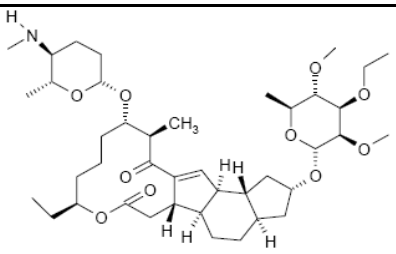
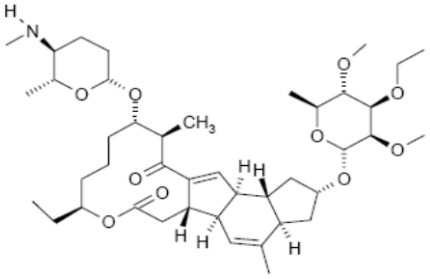
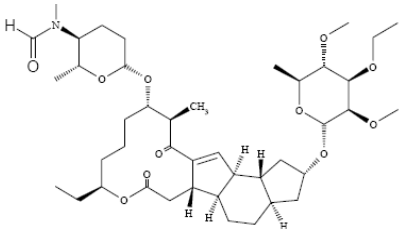
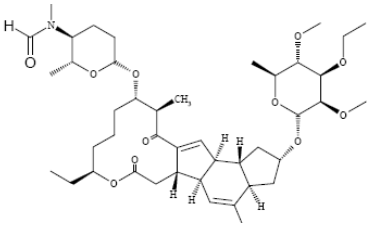
Tolerance/Maximum Residue Limit (ppm)

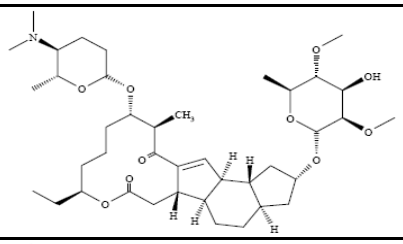
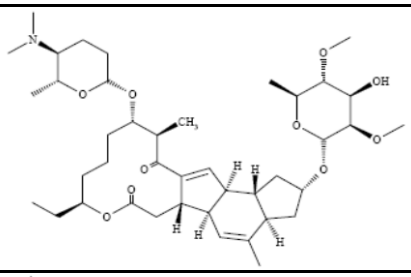
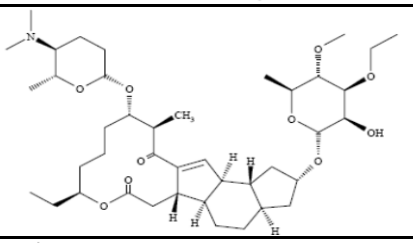
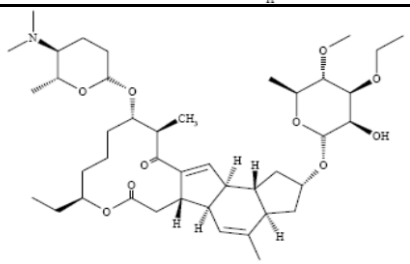
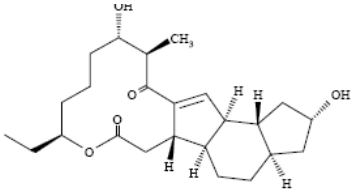
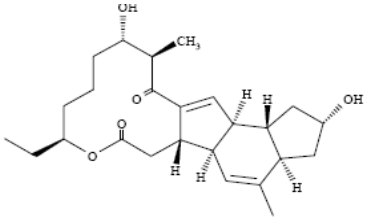
Commodity[1]	US	Canada	Mexico	Codex
strawberry, subgroup 13-07H				
Celtuce	8	0.04	8	-
Fennel, Florence, fresh leaves and stalk	8	8	8	-
Kohlrabi	2	0.04	0.3	2

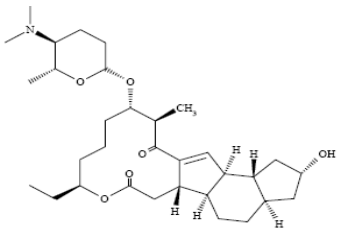
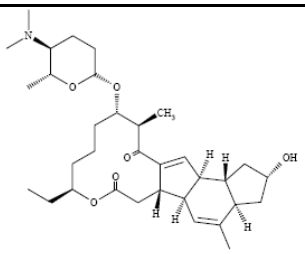
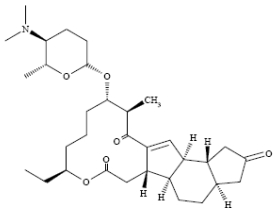
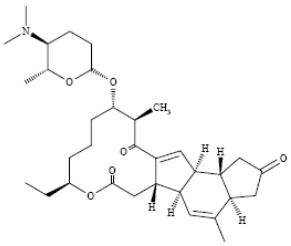
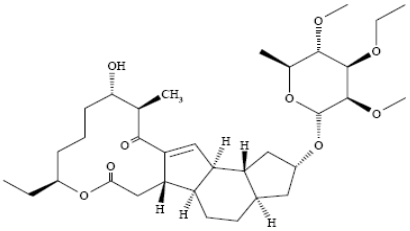
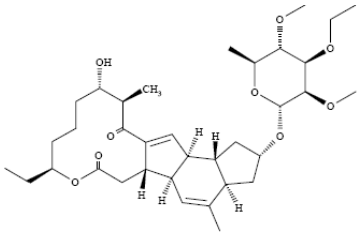
[1] Includes only commodities of interest for this action

Attachment 2: Chemical Names and Structures.

Spinosad	
Common name	Chemical structure
	
spinosyn A (parent)	**$R_1 = N(CH_3)_2$, $R_2 = H$, $R_3 = CH_3$, $R_4 = CH_3$, $R_5 = CH_3$**
spinosyn B (*N*-demethyl spinosyn A)	spinosyn A demethylated in the forosamine ring $R_1 = NH(CH_3)$, $R_2 = H$, $R_3 = CH_3$, $R_4 = CH_3$, $R_5 = CH_3$
spinosyn H (*O*-demethyl spinosyn A)	spinosyn A demethylated in the rhamose ring $R_1 = N(CH_3)_2$, $R_2 = H$, $R_3 = H$, $R_4 = CH_3$, $R_5 = CH_3$
spinosyn J (*O*-demethyl spinosyn A)	spinosyn A demethylated in the rhamose ring $R_1 = N(CH_3)_2$, $R_2 = H$, $R_3 = CH_3$, $R_4 = H$, $R_5 = CH_3$
spinosyn K (*O*-demethyl spinosyn A)	spinosyn A demethylated in the rhamose ring $R_1 = N(CH_3)_2$, $R_2 = H$, $R_3 = CH_3$, $R_4 = CH_3$, $R_5 = H$
N-demethyl spinosyn J	spinosyn J demethylated in the forosamine ring $R_1 = NH(CH_3)$, $R_2 = H$, $R_3 = CH_3$, $R_4 = H$, $R_5 = CH_3$
N-formyl spinosyn B	spinosyn A where one N-methyl group on the forosamine group has been removed and the other converted to CHO $R_1 = N(CH_3)(CHO)$, $R_2 = CH_3$, $R_3 = CH_3$, $R_4 = CH_3$, $R_5 = CH_3$
spinosyn D (parent)	**$R_1 = N(CH_3)_2$, $R_2 = CH_3$, $R_3 = CH_3$, $R_4 = CH_3$, $R_5 = CH_3$**
N-demethyl spinosyn D	spinosyn D demethylated in the forosamine ring $R_1 = NH(CH_3)$, $R_2 = CH_3$, $R_3 = CH_3$, $R_4 = CH_3$, $R_5 = CH_3$
spinosyn L (*O*-demethyl spinosyn D)	spinosyn D demethylated in the rhamose ring $R_1 = N(CH_3)_2$, $R_2 = CH_3$, $R_3 = CH_3$, $R_4 = H$, $R_5 = CH_3$
spinosyn O (*O*-demethyl spinosyn D)	spinosyn D demethylated in the rhamose ring $R_1 = N(CH_3)_2$, $R_2 = CH_3$, $R_3 = CH_3$, $R_4 = CH_3$, $R_5 = H$
spinosyn Q (*O*-demethyl spinosyn D)	spinosyn D demethylated in the rhamose ring $R_1 = N(CH_3)_2$, $R_2 = CH_3$, $R_3 = H$, $R_4 = CH_3$, $R_5 = CH_3$
N-demethyl spinosyn L	spinosyn L demethylated in the forosamine ring $R_1 = NH(CH_3)$, $R_2 = CH_3$, $R_3 = CH_3$, $R_4 = H$, $R_5 = CH_3$

Spinetoram		
Common name/code	Chemical name	Chemical structure
XDE-175-J	(2R,3aR,5aR,5bS,9S,13S,14R,16aS,16bR)-13-{[(2R,5S,6R)-5-(dimethylamino)-6-methyltetrahydro-2H-pyran-2-yl]oxy}-9-ethyl-14-methyl-7,15-dioxo-2,3,3a,4,5,5a,5b,6,7,9,10,11,12,13,14,15,16a,16b-octadecahydro-1H-as-indaceno[3,2-d]oxacyclododecin-2-yl 6-deoxy-3-O-ethyl-2,4-di-O-methyl-alpha-L-mannopyranoside	
XDE-175-L	(2S,3aR,5aS,5bS,9S,13S,14R,16aS,16bS)-13-{[(2R,5S,6R)-5-(dimethylamino)-6-methyltetrahydro-2H-pyran-2-yl]oxy}-9-ethyl-4,14-dimethyl-7,15-dioxo-2,3,3a,5a,5b,6,7,9,10,11,12,13,14,15,16a,16b-hexadecahydro-1H-as-indaceno[3,2-d]oxacyclododecin-2-yl 6-deoxy-3-O-ethyl-2,4-di-O-methyl-alpha-L-mannopyranoside	
N-demethyl-175-J ND-J	(2R,3aR,5aR,5bS,9S,13S,14R,16aS,16bR)-9-ethyl-14-methyl-13-{[(2S,5S,6R)-6-methyl-5-(methylamino)tetrahydro-2H-pyran-2-yl]oxy}-7,15-dioxo-2,3,3a,4,5,5a,5b,6,7,9,10,11,12,13,14,15,16a,16b-octadecahydro-1H-as-indaceno[3,2-d]oxacyclododecin-2-yl 6-deoxy-3-O-ethyl-2,4-di-O-methyl-alpha-L-mannopyranoside	
N-demethyl-175-L ND-L	(2S,3aR,5aS,5bS,9S,13S,14R,16aS,16bS)-9-ethyl-4,14-dimethyl-13-{[(2S,5S,6R)-6-methyl-5-(methylamino)tetrahydro-2H-pyran-2-yl]oxy}-7,15-dioxo-2,3,3a,5a,5b,6,7,9,10,11,12,13,14,15,16a,16bhexadecahydro-1H-as-indaceno[3,2-d]oxacyclododecin-2-yl 6-deoxy-3-O-ethyl-2,4-di-O-methyl-alpha-L-mannopyranoside	
N-formyl-175-J NF-J	(2R,3S,6S)-6-({(2R,3aR,5aR,5bS,9S,13S,14R,16aS,16bR)-2-[(6-deoxy-3-O-ethyl-2,4-di-O-methyl-alpha-L-mannopyranosyl) oxy]-9-ethyl-14-methyl-7,15-dioxo-2,3,3a,4,5,5a,5b,6,7,9,10,11,12,13,14,15,16a,16b-octadecahydro-1H-as-indaceno[3,2-d]oxacyclododecin-13-yl}oxy)-2-methyltetrahydro-2H-pyran-3-yl(methyl)formamide	
N-formyl-175-L NF-L	(2R,3S,6S)-6-({(2S,3aR,5aS,5bS,9S,13S,14R,16aS,16bS)-2-[(6-deoxy-3-O-ethyl-2,4-di-O-methyl-alpha-L-mannopyranosyl)oxy]-9-ethyl-4,14-dimethyl-7,15-dioxo-2,3,3a,5a,5b,6,7,9,10,11,12,13,14,15,16a,16b-hexadecahydro-1H-asindaceno[3,2-d]oxacyclododecin-13-yl}oxy)-2-methyltetrahydro-2H-pyran-3-yl(methyl)formamide	

Spinetoram		
Common name/code	Chemical name	Chemical structure
3'-O-deethyl-175-J	(2R,3aR,5aR,5bS,9S,13S,14R,16aS,16bR)-13-{[(2S,5S,6R)-5-(dimethylamino)-6-methyltetrahydro-2H-pyran-2-yl]oxy}-9-ethyl-14-methyl-7,15-dioxo-2,3,3a,4,5,5a,5b,6,7,9,10,11,12,13,14,15,16a,16b-octadecahydro-1H-as-indaceno[3,2-d]oxacyclododecin-2-yl 6-deoxy-2,4-di-O-methyl-alpha-L-mannopyranoside	
3'-O-deethyl-175-L	(2S,3aR,5aS,5bS,9S,13S,14R,16aS,16bS)-13-{[(2S,5S,6R)-5-(dimethylamino)-6-methyltetrahydro-2H-pyran-2-yl]oxy}-9-ethyl-4,14-dimethyl-7,15-dioxo-2,3,3a,5a,5b,6,7,9,10,11,12,13,14,15,16a,16bhexadecahydro-1H-as-indaceno[3,2-d] oxacyclododecin-2-yl 6-deoxy-2,4-di-O-methyl-alpha-L-mannopyranoside	
2'-O-demethyl-175-J	(2R,3aR,5aR,5bS,9S,13S,14R,16aS,16bR)-13-{[(2S,5S,6R)-5-(dimethylamino)-6-methyltetrahydro-2H-pyran-2-yl]oxy}-9-ethyl-14-methyl-7,15-dioxo-2,3,3a,4,5,5a,5b,6,7,9,10,11,12,13,14,15,16a,16b-octadecahydro-1H-as-indaceno[3,2-d] oxacyclododecin-2-yl 6-deoxy-3-O-ethyl-4-O-methyl-alpha-L-mannopyranoside	
2'-O-demethyl-175-L	(2S,3aR,5aS,5bS,9S,13S,14R,16aS,16bS)-13{[(2S,5S,6R)-5-(dimethylamino)-6-methyltetrahydro-2H-pyran-2-yl]oxy}-9-ethyl 4,14-dimethyl-7,15-dioxo-2,3,3a,5a,5b,6,7,9,10,11,12,13,14,15,16a,16b-hexadecahydro-1H-as-indaceno[3,2-d]oxacyclododecin-2-yl 6-deoxy-3-O-ethyl-4-O-methyl-alpha-L-mannopyranoside	
Aglycone-175-J	(2R,3aR,5aR,5bS,9S,13S,14R,16aS,16bR)-9-ethyl-2,13-dihydroxy-14-methyl-2,3,3a,4,5,5a,5b,6,9,10,11,12,13,14,16a,16b-hexadecahydro-1H-as-indaceno[3,2-d]oxacyclododecine-7,15-dione	
Aglycone-175-L	(2S,3aR,5aS,5bS,9S,13S,14R,16aS,16bS)-9-ethyl-2,13-dihydroxy-4,14-dimethyl-2,3,3a,5a,5b,6,9,10,11,12,13,14,16a,16b-tetradecahydro-1H-as-indaceno[3,2-d]oxacyclododecine-7,15-dione	

Spinetoram		
Common name/code	Chemical name	Chemical structure
C9-pseudoaglycone-175-J	(2R,3aR,5aR,5bS,9S,13S,14R,16aS,16bR)-13-{[(2S,5S,6R)-5-(dimethylamino)-6-methyltetrahydro-2H-pyran-2-yl]oxy}-9-ethyl-2-hydroxy-14-methyl-2,3,3a,4,5,5a,5b,6,9,10,11,12,13,14,16a,16b-hexadecahydro-1H-as-indaceno[3,2-d]oxacyclododecine-7,15-dione	
C9-pseudoaglycone-175-L	(2S,3aR,5aS,5bS,9S,13S,14R,16aS,16bS)-13-{[(2S,5S,6R)-5-(dimethylamino)-6-methyltetrahydro-2H-pyran-2-yl]oxy}-9-ethyl-2-hydroxy-4,14-dimethyl-2,3,3a,5a,5b,6,9,10,11,12,13,14,16a,16b-tetradecahydro-1H-as-indaceno[3,2-d]oxacyclododecine-7,15-dione	
C9-ketopseudoaglycone-175-J	(3aR,5aR,5bS,9S,13S,14R,16aS,16bR)-13-{[(2S,5S,6R)-5-(dimethylamino)-6-methyltetrahydro-2H-pyran-2-yl]oxy}-9-ethyl-14-methyl-3a,4,5,5a,5b,6,9,10,11,12,13,14,16a,16b-tetradecahydro-1H-as-indaceno[3,2-d]oxacyclododecine-2,7,15(3H)-trione	
C9-ketopseudoaglycone-175-L	(3aR,5aS,5bS,9S,13S,14R,16aS,16bS)-13-{[(2S,5S,6R)-5-(dimethylamino)-6-methyltetrahydro-2H-pyran-2-yl]oxy}-9-ethyl-4,14-dimethyl-3a,5a,5b,6,9,10,11,12,13,14,16a,16b-dodecahydro-1H-as-indaceno[3,2-d]oxacyclododecine-2,7,15(3H)-trione	
C17-ketopseudoaglycone-175-J	(2R,3aR,5aR,5bS,9S,13S,14R,16aS,16bR)-9-ethyl-13-hydroxy-14-methyl-7,15-dioxo-2,3,3a,4,5,5a,5b,6,7,9,10,11,12,13,14,15,16a,16b-octadecahydro-1H-asindaceno[3,2-d]oxacyclododecin-2-yl 6-deoxy-3-O-ethyl-2,4-di-O-methyl-alpha-Lmannopyranoside	
C17-ketopseudoaglycone-175-L	(2S,3aR,5aS,5bS,9S,13S,14R,16aS,16bS)-9-ethyl-13-hydroxy-4,14-dimethyl-7,15-dioxo-2,3,3a,5a,5b,6,7,9,10,11,12,13,14,15,16a,16b-hexadecahydro-1H-asindaceno[3,2-d]oxacyclododecin-2-yl 6-deoxy-3-O-ethyl-2,4-di-O-methyl-alpha-Lmannopyranoside	

Attachment 3: Tolerance Calculations (OECD).

Compound	SPINETORAM
Crop	DRAGON FRUIT
Region / Country	USA
GAP	
Total number of data (n)	4
Percentage of censored data	0%
Number of non-censored data	4
Lowest residue	0.087
Highest residue	0.640
Median residue	0.093
Mean	0.228
Standard deviation (SD)	0.275
Correction factor for censoring (CF)	1.000
Proposed MRL estimate	
- Highest residue	0.640
- Mean + 4 SD	1.326
- CF x 3 Mean	0.685
Unrounded MRL	1.326
Rounded MRL	1.5

High uncertainty of MRL estimate due to small dataset.

Residues (mg/kg)	
0.095	
0.087	
0.091	
0.640	

B.7.6 Residues Resulting from Supervised Trials (Annex IIA 6.3; Annex IIIA 8.3)

B.7.6.1 Residues in Target Crops

B.7.6.1.1 Dragon Fruit

Document ID: MRID No. 50854301

Report: Barney, W.P. (2017) Spinetoram: Magnitude of the Residue on Dragon Fruit (Pitaya). Study Numbers: 11514; 11514.15-FLR09. Unpublished study prepared and submitted by Interregional Research Project Number 4. 197 p.

Guidelines: EPA OCSPP Harmonized Test Guideline 860.1500 Crop Field Trials (August 1996)
PMRA Regulatory Directive DIR98-02 – Residue Chemistry Guidelines, Section 9 – Crop Field Trials
PMRA Regulatory Directive DIR2010-05 – Revisions to the Residue Chemistry Crop Field Trial Requirements
OECD Guideline 509 Crop Field Trial (September 2009)

GLP Compliance: No deviations from U.S. EPA regulatory requirements were reported which would have an impact on the validity of the study.

Acceptability: The study is considered scientifically acceptable. The acceptability of this study for regulatory purposes is addressed in the forthcoming U.S. EPA Residue Chemistry Summary Document, D461043

Evaluator: Oluwaseun Gbemigun, Ph.D.
Chemist, RAB1/HED (7509P)

Note: This Data Evaluation Record (DER) was prepared under contract by CDM/CSS-Dynamac Joint Venture (submitted 3/19/2020). The CDM/CSS-Dynamac Joint Venture role does not include establishing Agency policies. The DER has been reviewed by HED and revised as necessary to reflect current Office of Pesticide Programs (OPP) policies.

EXECUTIVE SUMMARY

Interregional Research Project Number 4 (IR-4) has submitted field trial data for spinetoram on dragon fruit (pitaya) from four field trials conducted in the United States during the 2015 and 2016 growing seasons. Trials were conducted in North American Free Trade Agreement (NAFTA) Growing Zone 13 (FL and HI).

Each trial consisted of one untreated plot and one treated plot reflecting four foliar directed applications of a 25% water-dispersible granule (WG) formulation of spinetoram at 0.094-0.101 lb ai/A/application, with retreatment intervals of 3-6 days, for total seasonal rates of 0.381-0.395 lb ai/A. Applications were made using ground equipment in dilute spray volumes of 123-133 gal/A at the three FL trials or in concentrated spray volumes of 45-47 gal/A at the HI trial. An adjuvant (nonionic surfactant or crop oil concentrate) was added to the spray mixture for each application at all trials. Duplicate samples of dragon fruit were harvested at a preharvest interval

(PHI) of 1 day. In one trial, samples were collected at additional PHIs of 0, 3, 7, 10, and 14 days to assess residue decline.

Samples were maintained frozen at the field sites, during shipping, and at the laboratory prior to analysis. The maximum storage interval for samples between harvest and extraction for analysis was 10.4 months. Samples were analyzed within 4 days of extraction. To support sample storage durations, a concurrent storage stability study was conducted using control samples of dragon fruit fortified with each analyte. The data demonstrate that residues of XDE-175-J, XDE-175-L, XDE-175-N-demethyl-J (ND-J), and XDE-175-N-formyl-J (NF-J) are stable during frozen storage in dragon fruit for at least 11.2 months. These data are acceptable to support the storage conditions and durations of the samples from the submitted field trials.

Samples were analyzed for residues of spinetoram, determined as XDE-175-J and XDE-175-L, and metabolites ND-J, and NF-J, using a method based on Dow AgroSciences Methods GRM 05.03 and GRM 05.04, high-performance liquid chromatography methods with tandem mass spectrometry detection (LC/MS/MS). Residues of all analytes (XDE-175-J, XDE-175-L, ND-J, and NF-J) were converted to spinetoram equivalents (a 3:1 mixture of XDE-175-J and XDE-175-L) by the study reviewer using molecular weight conversion factors (MWCFs) of 1.004 for XDE-175-J, 0.988 for XDE-175-L, 1.023 for ND-J, and 0.986 for NF-J. The limit of quantitation (LOQ; determined as the lowest level of method validation, LLMV) was 0.010 ppm for each analyte, and the combined LOQ was 0.040 ppm. Acceptable method validation and concurrent recoveries were obtained from samples of dragon fruit fortified with a mixed standard solution of XDE-175-J, XDE-175-L, ND-J, and NF-J, each at 0.010-1.0 ppm. The fortification levels adequately represented measured residue levels.

Following the last of four foliar directed applications totaling 0.381-0.395 lb ai/A, combined residues of XDE-175-J, XDE-175-L, ND-J, and NF-J in/on individual samples of dragon fruit harvested at a 1-day PHI were <0.085-0.673 ppm, and the corresponding per-trial average residues were 0.087-0.640 ppm. Average combined residues in/on samples from the HI trial, which utilized concentrated spray volumes, were substantially higher (0.640 ppm vs. 0.087-0.095 ppm, corresponding to 7x) than the average combined residues in/on samples from each of the other trials which used dilute spray volumes.

In the decline trial, average combined residues in/on dragon fruit decreased with increasing PHIs (PHIs 0 to 14 days).

I. MATERIALS AND METHODS

A. MATERIALS

Spinetoram, which consists of a mixture of XDE-175-J and XDE-175-L (J:L of 3:1), is derived from synthetic modification of *Saccharopolyspora spinosa* fermentation products.

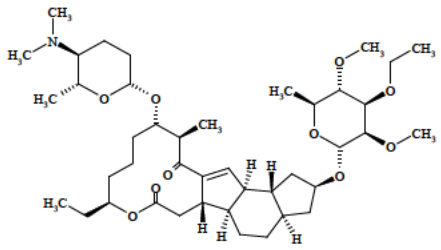
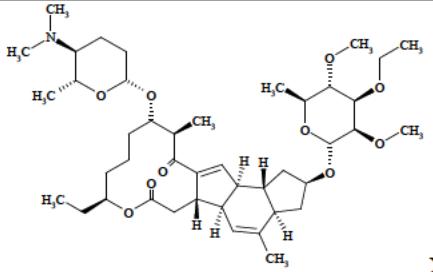
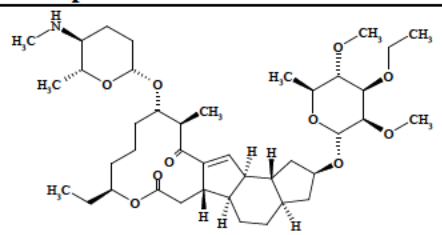
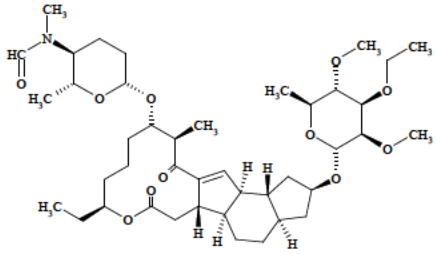
Table B.7.6.1.1-1. Nomenclature for Spinetoram and Metabolites.	
Common name	Spinetoram (mixture of XDE-175-J and XDE-175-L)
IUPAC name	**XDE-175-J:** (2*R*,3a*R*,5a*R*,5b*S*,9*S*,13*S*,14*R*,16a*S*,16b*R*)-13-{[(2*R*,5*S*,6*R*)-5-(dimethylamino)-6-methyltetrahydro-2*H*-pyran-2-yl]oxy}-9-ethyl-14-methyl-7,15-dioxo-2,3,3a,4,5,5a,5b,6,7,9,10,11,12,13,14,15,16a,16b-octadecahydro-1*H*-as-indaceno[3,2-*d*]oxacyclododecin-2-yl 6-deoxy-3-*O*-ethyl-2,4-di-*O*-methyl-alpha-*L*-mannopyranoside **XDE-175-L:** (2*S*,3a*R*,5a*S*,5b*S*,9*S*,13*S*,14*R*,16a*S*,16b*S*)-13-{[(2*R*,5*S*,6*R*)-5-(dimethylamino)-6-methyltetrahydro-2*H*-pyran-2-yl]oxy}-9-ethyl-4,14-dimethyl-7,15-dioxo-2,3,3a,5a,5b,6,7,9,10,11,12,13,14,15,16a,16b-hexadecahydro-1*H*-as-indaceno[3,2-*d*]oxacyclododecin-2-yl 6-deoxy-3-*O*-ethyl-2,4-di-*O*-methyl-alpha-*L*-mannopyranoside
CAS name	**XDE-175-J:** 1*H*-as-indaceno[3,2-*d*]oxacyclododecin-7,15-dione, 2-[(6-deoxy-3-*O*-ethyl-2,4-di-*O*-methyl-a-*L*-mannopyranosyl)oxy]-13-[[(2*R*,5*S*,6*R*)-5-(dimethylamino)tetrahydro-6-methyl 2*H*-pyran-2-yl]oxy]-9-ethyl-2,3,3a,4,5,5a,5b,6,9,10,11,12,13,14,16a,16b-hexadecahydro 14-methyl-(2*R*,3a*R*,5a*R*,5b*S*,9*S*,13*S*,14*R*,16a*S*,16b*R*) **XDE-175-L:** 1*H*-as-indaceno[3,2-*d*]oxacyclododecin-7,15-dione,2-[(6-deoxy-3-*O*-ethyl-2,4-di-*O*-methyl-a-*L*-mannopyranosyl)oxy]-13-[[(2*R*,5*S*,6*R*)-5-(dimethylamino)tetrahydro-6-methyl-2*H*-pyran-2-yl]oxy]-9-ethyl-2,3,3a,5a,5b,6,9,10,11,12,13,14,16a,16b-tetradecahydro-4,14-dimethyl-(2*S*,3a*R*,5a*S*,5b*S*,9*S*,13*S*,14*R*,16a*S*,16b*S*)
CAS registry number	**XDE-175-J:** 187166-40-1; **XDE-175-L:** 187166-15-0
Molecular weight	**XDE-175-J:** 748.02 g/mol; **XDE-175-L:** 760.03 g/mol
Company experimental name	**XDE-175-J:** TSN104472; 3'-O-ethyl 5,6-dihydro spinosyn J; 175-J **XDE-175-L:** TSN104480; 3'-O-ethyl spinosyn L; 175-L
 XDE-175-J	 XDE-175-L
Metabolite name	XDE-175-N-demethyl-J
Identity	(2*R*,3a*R*,5a*R*,5b*S*,9*S*,13*S*,14*R*,16a*S*,16b*R*)-9-ethyl-14-methyl-13[[(2*S*,5*S*,6*R*)-6-methyl-5-(methylamino)tetrahydro-2*H*-pyran-2-yl]oxy]-7,15-dioxo-2,3,3a,4,5,5a,5b,6,7,9,10,11,12,13,14,15,16a,16b-octadecahydro-1*H*-as-indaceno[3,2-*d*]oxacyclododecin-2-yl-6-deoxy-3-O-ethyl-2,4-di-O-methyl-α-*L*-mannopyranoside
Molecular weight	733.97 g/mol
Other synonyms	ND-J

Table B.7.6.1.1-1. Nomenclature for Spinetoram and Metabolites.	
	
Metabolite name	XDE-175-N-formyl-J
Identity	(2*R*,3*S*,6*S*)-6-([(2*R*,3a*R*,5a*R*,5b*S*,9*S*,13*S*,14*R*,16a*S*,16b*R*)-2-[(6-deoxy-3-O-ethyl-2,4-di-O-methyl-α-L-mannopyranosyl)oxy]-9-ethyl-14-methyl-7,15-dioxo-2,3,3a,4,5,5a,5b,6,7,9,10,11,12,13,14,15,16a,16b-octadecahydro-1*H*-as-indaceno[3,2-*d*]oxacyclododecin-13-yl]oxy)-2-methyltetrahydro-2*H*-pyran-3-yl(methyl)formamide
Molecular weight	762.00 g/mol
Other synonyms	NF-J
	

B. Study Design

1. Test Procedure

Four field trials on dragon fruit were conducted with a WG formulation during the 2015 and 2016 growing seasons. Field trial locations by NAFTA growing zone are summarized in Table B.7.6.1.1-2.

All trials, except for those listed in the table below, were separated by ≥20 miles, or were conducted in different years, and are therefore considered independent (568_Criteria for Independence of Trials 4/23/13 (EPA and PMRA)). The trials separated by <20 miles have been assessed for independence as detailed in the table below. HED determined that there are sufficient differences between the trials that they may be considered separate.

Independent Trial Determination[1]		
Trial Nos. 11514.15-	Differences	Decision
FL166 and FL167	Location: Same site Variety: Rosa (both) Timing: First applications separated by 46 days Spray Volume: 130-133 vs 125-127 GPA Adjuvant: NIS (both)	Separate due to timing

[1] All assessments are based on the replicate trial guidance presented in draft memo 568_Criteria for Independence of Trials 4/23/13 (EPA and PMRA).

Table B.7.6.1.1-2. Trial Numbers and Geographical Locations.															
Crop	No. Trials	NAFTA Growing Zone													Total
		1	2	3	4	5	6	7	8	9	10	11	12	13	
Dragon fruit	Sub.													4	4
	Req.[1]														

[1] Guideline 860.1500 does not specify trial numbers or locations for dragon fruit.

Locations and detailed use patterns for the trials are provided in Table B.7.6.1.1-3. Foliar directed applications were made in dilute spray volumes at the three FL trials and in concentrated spray volumes at the HI trial.

Table B.7.6.1.1-3. Study Use Pattern.							
Location: City, State; Year (Trial ID 11514.)	End-use Product[1]	Method of Application; Timing of Application	Volume (gal/A)	Rate per Application (lb ai/A)	Retreatment Interval (days)	Total Rate (lb ai/A)	Surfactant/ Adjuvant[2]
Homestead, FL; 2015 (15-FL166)	25% WG	1. Foliar directed; fruiting	131	0.0985	--	0.395	NIS
		2. Foliar directed; fruiting	130	0.0980	3		
		3. Foliar directed; fruiting	133	0.1004	3		
		4. Foliar directed; fruiting	130	0.0981	3		
Homestead, FL; 2015 (15-FL167)	25% WG	1. Foliar directed; fruiting	127	0.0959	--	0.381	NIS
		2. Foliar directed; fruiting	125	0.0945	3		
		3. Foliar directed; fruiting	127	0.0958	4		
		4. Foliar directed; fruiting	126	0.0950	6		
Homestead, FL; 2016 (16-FL518)	25% WG	1. Foliar directed; bloom, fruiting	130	0.1014	--	0.394	COC
		2. Foliar directed; bloom, fruiting	128	0.0998	5		
		3. Foliar directed; fruiting	124	0.0966	4		
		4. Foliar directed; fruiting	123	0.0958	3		
Waialua, HI; 2015 (15-HI204)	25% WG	1. Foliar directed; fruiting	46	0.0959	--	0.383	NIS
		2. Foliar directed; fruiting	47	0.0968	4		
		3. Foliar directed; fruiting	46	0.0962	3		
		4. Foliar directed; fruiting	45	0.0942	4		

[1] A 25% WG formulation of spinetoram (Delegate WG).
[2] NIS = Nonionic surfactant; COC = Crop oil concentrate.

Dragon fruits were grown and maintained using typical agricultural practices. Irrigation was used at all trials, but was not used between the first application and harvest at Trial HI204. No unusual weather conditions were reported to have adversely affected crop growth or yields during the study.

Sample Handling and Preparation

Duplicate untreated and treated samples of dragon fruit were collected from all trials at a 1-day PHI, except for untreated samples from the decline trial, which were collected at the 0-day PHI. At the decline trial (Trial FL166), additional treated samples were harvested at PHIs of 0, 3, 7, 10, and 14 days to assess residue decline. Samples were placed in frozen storage (generally <-17 °C) at the field sites within 1.5 hours of collection and were shipped by freezer truck or overnight courier on dry ice to the analytical laboratory, IR-4 Southern Region Laboratory, University of Florida (Gainesville, FL). At the laboratory, samples were homogenized in the presence of dry ice and stored frozen (generally <0 °C) until extraction for analysis.

2. Description of Analytical Procedures

Samples were analyzed for residues of XDE-175-J, XDE-175-L, ND-J, and NF-J using an LC/MS/MS method based on Dow AgroSciences Methods GRM 05.03 and GRM 05.04. A complete description of the method, including modifications, was included in the submission. Modifications included elimination of internal standards and the C-18 solid phase extraction cleanup step, and isolation of the final extract by filtration instead of centrifugation.

Briefly, samples were extracted with acetonitrile:water (80:20, v:v) with shaking for at least 30 minutes. Extracts were then filtered through a 0.2-µm PTFE syringe filter for analysis by LC/MS/MS. Slightly different LC/MS/MS systems were used for analysis of samples from the 2015 trials (analyzed in 2016) and 2016 trial (analyzed in 2017); the following transitions were monitored:

Analyte	Ion Transition (2016 analyses)	Ion Transition (2017 analyses)
XDE-175-J	*m/z* 748.4 → 142.2	*m/z* 748.461 → 142.146
XDE-175-L	*m/z* 760.4 → 142.2	*m/z* 760.552 → 142.075
ND-J	*m/z* 734.4 → 128.2	*m/z* 734.430 → 128.146
NF-J	*m/z* 762.4 → 156.1	*m/z* 762.552 → 156.100

The LOQ (determined as the LLMV) was 0.010 ppm for each analyte. The study author also presented calculated values for the limit of detection (LOD) and LOQ for each analyte based on recoveries obtained at the LLMV fortification level. The LOD was calculated by multiplying the standard deviation of recovery measurements at the LLMV by the one-tailed t-statistic (99% confidence level) for 6 replicates, and the LOQ was defined as 3x the LOD. The calculated LOQ and LOD, respectively, were 0.0078 and 0.0026 ppm for XDE-175-J, 0.0089 and 0.0030 ppm for XDE-175-L, 0.0102 and 0.0034 ppm for ND-J, and 0.0076 and 0.0025 ppm for NF-J.

Residues of all analytes (XDE-175-J, XDE-175-L, ND-J, and NF-J) were converted to spinetoram equivalents (a 3:1 mixture of XDE-175-J and XDE-175-L) by the study reviewer using MWCFs (MW spinetoram ÷ MW metabolite) of 1.004 for XDE-175-J, 0.988 for XDE-175-L, 1.023 for ND-J, and 0.986 for NF-J. The combined LOQ was 0.040 ppm.

II. RESULTS AND DISCUSSION

Method performance was evaluated by use of method validation and concurrent recovery samples of dragon fruit fortified with a mixed standard solution of XDE-175-J, XDE-175-L, ND-J, and NF-J, each at 0.010-1.0 ppm. Recoveries were generally within the acceptable range of 70-120%; therefore, the method is considered valid for the determination of residues of XDE-175-J, XDE-175-L, ND-J, and NF-J in/on dragon fruit (Table B.7.6.1.1-4). The fortification levels adequately represented the measured residues. Concurrent recoveries were not corrected for apparent residues in/on controls.

The detector response was linear (coefficient of determination, $r^2 \geq 0.9742$) within the range of 0.25-25 ng/mL. Representative chromatograms of control samples, fortified samples, and treated samples were provided. The control chromatograms generally had no peaks of interest above the

chromatographic background. The fortified sample chromatograms contained only the analyte of interest, and peaks were symmetrical and well defined. Apparent residues were below the LOQ (<0.010 ppm) in/on all controls.

Table B.7.6.1.1-4. Summary of Method Validation and Concurrent Recoveries of XDE-175-J, XDE-175-L, ND-J, and NF-J from Dragon Fruit.

Matrix	Analyte	Fortification Level (ppm)	Sample Size (n)	Recoveries[1] (%)	Mean ± Std. Dev. (%)
Method Validation					
Dragon fruit	XDE-175-J	0.010-1.0	12	67, 68; 70-97	85 ± 11
	XDE-175-L	0.010-1.0	12	74-95	83 ± 7
	ND-J	0.010-1.0	12	69; 70-94	80 ± 9
	NF-J	0.010-1.0	12	83-96	88 ± 3
Concurrent Recovery					
Dragon fruit	XDE-175-J	0.010, 1.0	4	97-104	99 ± 3
	XDE-175-L	0.010, 1.0	4	89-99	94 ± 4
	ND-J	0.010, 1.0	4	83-101	94 ± 8
	NF-J	0.010, 1.0	4	82-102	95 ± 9

[1] Concurrent recoveries were not corrected for apparent residues in controls.

The maximum storage interval for samples between harvest and extraction for analysis was 10.4 months (Table B.7.6.1.1-5a). Samples were analyzed within 4 days of extraction. To support sample storage durations, a concurrent storage stability study was conducted using untreated samples of dragon fruit from Trial FL167 fortified with a mixed standard solution of XDE-175-J, XDE-175-L, ND-J, and NF-J at 0.1 ppm each; no 0-day data were provided. The data demonstrate that residues of XDE-175-J, XDE-175-L, ND-J, and NF-J are stable during frozen storage in dragon fruit for at least 11.2 months (Table B.7.6.1.1-5b). These data are acceptable to support the storage conditions and durations of the samples from the submitted field trials.

Table B.7.6.1.1-5a. Summary of Storage Conditions.

Matrix	Storage Temperature (°C)	Actual Storage Duration[1]	Interval of Demonstrated Storage Stability
Dragon fruit	<0	114-318 days (3.7-10.4 months)	Residues of XDE-175-J, XDE-175-L, ND-J, and NF-J are stable in dragon fruit during frozen storage for at least 11.2 months.[2]

[1] Interval from harvest to extraction. Samples were analyzed within 0-4 days of extraction.
[2] Concurrent storage stability study; refer to Table B.7.6.1.1-5b.

Table B.7.6.1.1-5b. Stability of XDE-175-J, XDE-175-L, ND-J, and NF-J Residues in Dragon Fruit During Frozen Storage (<0 °C).

Analyte	Spike Level (ppm)	Storage Interval, days (months)	Fresh Fortification Recovery (%)	Stored Sample Recoveries (%)	Mean Recovery (%)	Corrected % Recovery[1]
XDE-175-J	0.1[2]	342 (11.2)	96	83, 88, 88	86	90
XDE-175-L			94	82, 81, 84	82	88
ND-J			97	73, 70, 73	72	74
NF-J			95	93, 97, 91	94	99

[1] Corrected for recovery in freshly fortified samples.
[2] Fresh fortification samples were fortified with each analyte at 1 ppm.

The results from the submitted field trials are presented in Table B.7.6.1.1-6 and summarized in Table B.7.6.1.1-7. Following foliar applications of spinetoram at a total rate of 0.381-0.395 lb ai/A, combined residues of XDE-175-J, XDE-175-L, ND-J, and NF-J were <0.085-0.673 ppm

in/on dragon fruit harvested at a 1-day PHI. Average combined residues in/on samples from the HI trial, reflecting concentrated spray volumes, were substantially higher (0.640 ppm vs. 0.087-0.095 ppm; corresponding to 7x) than the average combined residues in/on samples from each of the FL trials which reflected dilute spray volumes.

In the residue decline trial, mean combined residues of XDE-175-J, XDE-175-L, ND-J, and NF-J in/on dragon fruit decreased from 0.129 ppm at the 0-day PHI to <0.042 ppm at the 14-day PHI (Figure 7.6.1.1-1).

Table B.7.6.1.1-6. Residue Data from Dragon Fruit Field Trials with Spinetoram.[1]

Location: City, State; Year (Trial ID 11413.)	Zone	Crop Variety	Matrix	Rate (lb ai/A)	Spray Volume[2]	PHI (days)	Residues[3] (ppm spinetoram equivalents) [Average]				
							XDE-175-J	XDE-175-L	ND-J	NF-J	Combined[4]
Homestead, FL; 2015 (15-FL166)	13	Rosa	Fruit	0.395	Dilute	0	0.059, 0.057 [0.058]	0.021, 0.021 [0.021]	0.023, 0.022 [0.022]	0.028, 0.027 [0.028]	0.131, 0.127 [0.129]
						1	0.029, 0.035 [0.032]	0.012, 0.013 [0.012]	0.017, 0.019 [0.018]	0.033, 0.033 [0.033]	0.090, 0.100 [0.095]
						3	0.028, 0.021 [0.025]	0.011, <0.010 [<0.010]	0.019, 0.014 [0.017]	0.035, 0.032 [0.033]	0.093, <0.077 [<0.085]
						7	0.017, 0.012 [0.015]	<0.010, <0.010 [<0.010]	0.012, <0.010 [<0.011]	0.019, 0.013 [0.016]	<0.058, <0.045 [<0.052]
						10	0.011, 0.015 [0.013]	<0.010, <0.010 [<0.010]	<0.010, 0.010 [<0.010]	0.010, 0.016 [0.013]	<0.041, <0.051 [<0.046]
						14	<0.010, <0.010 [<0.010]	<0.010, <0.010 [<0.010]	<0.010, <0.010 [<0.010]	0.013, <0.010 [<0.011]	<0.043, <0.040 [<0.042]
Homestead, FL; 2015 (15-FL167)	13	Rosa	Fruit	0.381	Dilute	1	0.037, 0.033 [0.035]	0.011, 0.012 [0.012]	0.015, 0.014 [0.015]	0.026, 0.026 [0.026]	0.089, 0.085 [0.087]
Homestead, FL; 2016 (16-FL518)	13	Rosa	Fruit	0.394	Dilute	1	0.015, 0.014 [0.015]	<0.010, <0.010 [<0.010]	<0.010, <0.010 [<0.010]	0.049, 0.062 [0.056]	<0.085, <0.097 [<0.091]
Waialua, HI; 2015 (15-HI204)	13	Kona Brazil	Fruit	0.383	Concentrate	1	0.162, 0.161 [0.161]	0.043, 0.042 [0.043]	0.101, 0.089 [0.095]	0.368, 0.314 [0.341]	0.673, 0.606 [0.640]

[1] A 25% WG formulation of spinetoram (Delegate WG) was used.

[2] Application sprays were made using concentrated (45-47 GPA) or dilute (123-133 GPA) spray volumes.

[3] The LOQ was 0.010 ppm for each analyte. Per-trial averages and combined residues were calculated by the study reviewer using the LOQ for all residues reported as <LOQ. All residues were converted to spinetoram equivalents (a 3:1 mixture of XDE-175-J and XDE-175-L) by the study reviewer using MWCFs of 1.004 for XDE-175-J, 0.988 for XDE-175-L, 1.023 for ND-J, and 0.986 for NF-J

[4] Combined residues of XDE-175-J, XDE-175-L, ND-J, and NF-J. The combined LOQ was 0.040 ppm.

Figure B.7.6.1.1-1. Combined Spinetoram Residues in/on Dragon Fruit at Various PHIs.

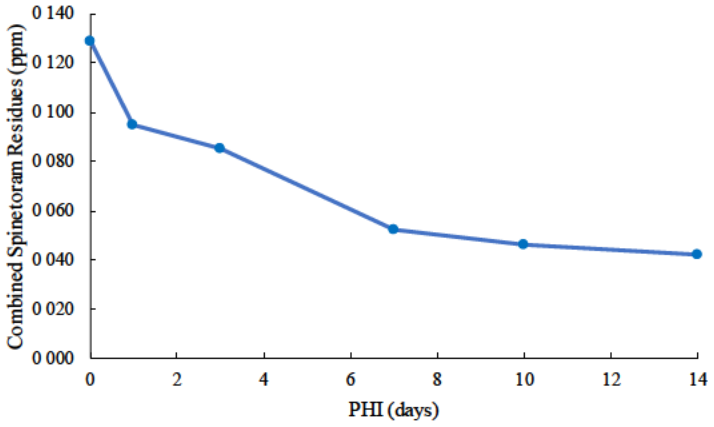


Table B.7.6.1.1-7. Summary of Residues from Dragon Fruit Field Trials with Spinetoram.

Crop Matrix	Analyte	Total Application Rate (lb ai/A)	PHI (days)	n[1]	Residues (ppm spinetoram equivalents)						
					Min.[2]	Max.[2]	LAFT[3]	HAFT[3]	Median[3]	Mean[3]	SD[3]
Dragon fruit	XDE-175-J	0.381-0.395	3	4	0.014	0.162	0.015	0.161	0.033	0.061	0.068
	XDE-175-L			4	<0.010	0.043	<0.010	0.043	0.012	0.019	0.016
	ND-J			4	<0.010	0.101	<0.010	0.095	0.016	0.034	0.040
	NF-J			4	0.026	0.368	0.026	0.341	0.044	0.114	0.152
	Combined[4]			4	<0.085	0.673	0.087	0.640	0.093	0.228	0.274

[1] n = number of independent field trials.
[2] Values based on residues in individual samples.
[3] Values based on per-trial averages. LAFT = lowest average field trial, HAFT = highest average field trial, SD = standard deviation. For computation of the LAFT, HAFT, median, mean, and standard deviation, values <LOQ are assumed to be at the LOQ (0.010 ppm for each analyte).
[4] Combined residues of XDE-175-J, XDE-175-L, ND-J, and NF-J.

III. CONCLUSIONS

The dragon fruit field trials are considered scientifically acceptable. Following four foliar directed applications of spinetoram at a total rate of 0.381-0.395 lb ai/A, combined residues of XDE-175-J, XDE-175-L, ND-J, and NF-J were <0.085-0.673 ppm in/on dragon fruit samples harvested at a 1-day PHI. Average combined residues in/on samples from the HI trial, reflecting concentrate spray volumes, were higher (0.640 ppm vs. 0.087-0.095 ppm; corresponding to 7x) than the average combined residues in/on samples from the other trials which reflected dilute spray volumes.

In the decline trial, average combined residues in/on dragon fruit decreased with increasing PHIs (PHIs 0 to 14 days).

An acceptable method was used for residue quantitation, and adequate storage stability data were submitted to support sample storage durations and conditions for all analytes.

REFERENCES

None