MRID: 51169901

TITLE:

FLUENSULFONE:

MINOR USE REGISTRATIONS PETITION FOR 3 YEAR EXTENSION OF EXCLUSIVITY USE DATA PROTECTION PROVIDED UNDER FIFRA SECTION 3(c) (1) (F) (ii)

AUTHORS

Claire M. Koenig, PhD

Pablo Navia, PhD

Miriam Frugis, MSc

GUIDELINE REFERENCE

None

COMPLETION DATE

May 28, 2020

PERFORMING LABORATORY:

Not Applicable

PROJECT IDENTIFICATION NUMBER:

Not Applicable

SPONSOR:

ADAMA USA

c/o Makhteshim Agan of North America (d/b/a ADAMA)

3120 Highwoods Boulevard, Suite 100, Raleigh NC 27604

STATEMENT OF DATA CONFIDENTIALITY CLAIMS

No claim of confidentiality, on any basis whatsoever, is made for any information contained in this document. I acknowledge that this information is not designated as within the scope of FIFRA sec. 10(d)(1)(A), (B), or (C), which pertains to a registered or previously registered pesticide and is not entitled to confidential treatment. It may be released to the public, subject to the provisions regarding disclosure to multinational entities under FIFRA sec. 10(g).

SUBMITTER:

SIGNATURE: [signature] **DATE:** MAY 28, 2020

NAME: Miriam Frugis

TITLE: Federal Registration Manager

COMPANY: ADAMA USA
c/o Makhteshim Agan of North America (d/b/a ADAMA)
3120 Highwoods Boulevard, Suite 100, Raleigh NC 27604

STATEMENT OF COMPLIANCE WITH GOOD LABORATORY PRACTICE STANDARDS

This report is a review of existing data. Good Laboratory Practice Standards, 40 CFR Part 160, are not applicable to this submission.

__________________________________ **DATE:** MAY 28, 2020

SPONSOR/SUBMITTER: Miriam Frugis
Federal Registration Manager
ADAMA USA
c/o Makhteshim Agan of North America (d/b/a ADAMA)

1. INTRODUCTION

Makhteshim Agan of North America, Inc. (d/b/a ADAMA) respectfully petitions EPA to extend the period of exclusive data use for Fluensulfone nematicide by 3 years, by applying the provision of FIFRA Section 3(c) (1) (F) (ii).

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

> *The period of exclusive data use provided under clause (i) shall be extended 1 additional year for each 3 minor uses registered after the date of enactment of this clause and within 7 years of the commencement of the exclusive use period, up to a total of 3 additional years for all minor uses registered by the Administrator if the Administrator, in consultation with the Secretary of Agriculture, determines that, based on information provided by an applicant for registration or a registrant, that –*
>
> *(I) there are insufficient efficacious alternative registered pesticides available for the use;*
>
> *(II) the alternatives to the minor use pesticide pose greater risks to the environment or human health;*
>
> *(III) the minor use pesticide plays or will play a significant part in managing pest resistance;*
>
> *(IV) the minor use pesticide plays or will play a significant part in an integrated pest management* program.

Details of how fluensulfone meets at least one of the four qualifying criteria for the proposed minor crop uses are described in the following sections.

2. FLUENSULFONE REGISTRATIONS

Fluensulfone technical (EPA Reg. No. 11678-73), or MCW-2, (5-chloro-2-(3,4,4-trifluorobut-3-enylsulfonyl)-1,3-thiazole), was first registered by the US EPA on September 11th, 2014. The formulation of fluensulfone – Fluensulfone 480 EC (i.e. Nimitz®; EPA Reg. No. 66222-243) contains 4 pounds of fluensulfone per gallon and is registered and approved for use in a variety of crops including the following minor use crops detailed in this document: strawberry, carrot, radish, sweet potato, cherry, peach, watermelon, cantaloupe, okra, pepper, kiwi, macadamia, and pecan (Fluensulfone 480 EC Label).

Fluensulfone in its formulated product Fluensulfone 480 EC provides control of against a wide variety of plant parasitic nematodes (PPNs): Root-knot (*Meloidogyne* spp.), Potato cyst (*Globodera* spp.), Needle (*Longidorus africanus*), Lance (*Hoplolaimus* spp.), Sting (*Belonolaimus* spp.), Stubby Root (*Trichodorus* and *Paratrichodorus* spp.), and Lesion (*Pratylenchus* spp.).

In some instances, the active ingredient is already acting commercially as a viable substitute for other pesticidal options or other control measures which pose a greater risk to human safety and/or the environment, including the less desirable and hazardous soil fumigants (e.g. metam solidum, 1,3-dichloropropene and chloropicrin) and acetylcholine esterase inhibitors (e.g. oxamyl). Fluensulfone 480 EC has a minimally restrictive "CAUTION" labelling, a short 12 hour restricted-entry interval (REI) for all uses which means no handling restrictions and less complicated personal protective equipment requirements than for fumigant products (Navia, 2014a; Appendix 1– Fluensulfone 480 EC Label). There is also no need for fumigant management plans, restrictive buffer zones, and long re-entry intervals (Navia, 2014b).

3. FLUENSULFONE MODE OF ACTION

Fluensulfone is a pyrazole nematicide and is the first nematicide in the fluoroalkenyl class (Phillion et al., 1999; Oka et al., 2008; Oka et al., 2009). It targets Root-knot (Meloidogyne spp.), Potato cyst (*Globodera* spp.), Needle (*Longidorus africanus*), Lance (*Hoplolaimus* spp.), Sting (*Belonolaimus* spp.), stubby root (*Trichodorus* and *Paratrichodorus* spp.), and Lesion (*Pratylenchus* spp.).

Fluensulfone has a pleiotropic expression of activity against nematodes that includes weak inhibition of motility in adults, strong inhibition of motility in larvae, feeding inhibition and egg-laying, hatching and developmental inhibition. Inhibition of larval thrashing and feeding is irreversible after 24 hours of exposure and the cuticle does not appear to prevent access of fluensulfone (EPA, 2014; Kearn et al., 2014).

Fluensulfone, unlike other chemical controls, presents with relatively low toxicity to non-target organisms (Navia 2014a; Kearn et al., 2014 Oka et al., 2009). A comparison of the different nematicide active ingredients is present in Appendix 1.

4. MINOR USE CROP REGISTRATIONS FOR FLUENSULFONE THAT QUALIFY FOR EXCLUSIVITY USE DATA PROTECTION

Table 1. Fluensulfone Minor Uses for Exclusivity Period Extension

Crop Group	MINOR CROP REGISTRATION	PLANTED ACRES IIN 2017	REGISTRATION DATE	NEMATODE(S) CONTROLLED BY FLUENSULFONE	FUFILL DATA EXTENSION CRITERIA*
1B	**Carrot** *Daucus carota*	74,513	June 06, 2016	*Meloidogyne* spp. (root-knot nematode) *Pratylenchus* spp. (lesion nematode)	II, III and IV
1C	**Sweet Potato** *Ipomoea batatas*	132,220	June 06, 2016	*Meloidogyne* spp. (root-knot nematode)	II, III and IV
8-10	**Okra** *Abelmoschus esculentus* (L.) Moench	3,085	December 09, 2014	*Meloidogyne* spp. (root-knot nematode)	II, III and IV
8-10	**Pepper, bell** *Capsicum annuum* L. var. *annuum*, *Capsicum* spp	43,685	December 09, 2014	*Meloidogyne* spp. (root-knot nematode), *Pratylenchus* spp. (lesion nematode); *Belonolaimus longicaudatus* (sting nematode)	II, III and IV
9	**Watermelon** *Citrullus lanatus*	127,133	December 09, 2014	*Meloidogyne* spp. (root-knot nematode) *Pratylenchus* spp. (lesion nematode) *Trichodorus* spp. (stubby-root nematode)	II, III and IV
9	**Cantaloupe** *Citrullus melo*	71,201	December 09, 2014	*Meloidogyne* spp. (root-knot nematode) *Pratylenchus* spp. (lesion nematode); *Trichodorus* spp. (stubby-root nematode)	II, III and IV
12-12	**Cherry, sweet** *Prunus avium* (L.) L.	105,978	April 24, 2018	*Meloidogyne* spp. (root-knot nematode)	II, III and IV
12-12	**Peach** *Prunus persica* (L.) Batsch var. *persica*	112,861	April 24, 2018	*Meloidogyne* spp. (root-knot nematode) *Mesocriconema spp.* (ring nematode)	II, III and IV
13-07G	**Strawberry** *(Fragaria ananassa* Duchesne*)*	60,162	June 06, 2016	*Meloidogyne* spp. (root-knot nematode) *Pratylenchus* spp. (lesion nematode) *Belonolaimus longicaudatus* (sting nematode)	II, III and IV
13-07D	**Kiwi** *Actinidia deliciosa* A. Chev.) (C.F. Liang and A.R. Fergusons, *Actinida chinensis* Planch.	4,554	April 24, 2018	*Meloidogyne* spp. (root-knot nematode)	II, III and IV

Crop Group	MINOR CROP REGISTRATION	PLANTED ACRES IIN 2017	REGISTRATION DATE	NEMATODE(S) CONTROLLED BY FLUENSULFONE	FUFILL DATA EXTENSION CRITERIA*
14-12	**Macadamia** *Macadamia* spp.	18,403	April 24, 2018	*Meloidogyne* spp. (root-knot nematode)	II, III and IV
14-12	**Pecan** *Carya illinoensis*	155,678	April 24, 2018	*Meloidogyne* spp. (root-knot nematode)	II, III and IV

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

Details of how fluensulfone meets the exclusivity criteria for each minor use are provided in the following sections

5. JUSTIFICATION OF THE NEED FOR FLUENSULFONE TO CONTROL PLANT PARASITIC NEMATODES.

Competitor analysis presented for carrots applies for all the minor crops presented in this document.

a. Carrot

Carrots, a cool-season crop that is always direct seeded. Roots attain optimal color when the air temperature is 60° to 70°F. Although carrots are available year-round, locally grown carrots are in season in the summer and fall when they are freshest and most flavorful. In 2015, fresh market carrots were harvested from 71,550 acres with a total yield of approximately 2.4 billion pounds. Carrots are grown in and shipped through-out the year from California which produces about 85% of all carrots grown in the United States. Michigan and Texas are the other important carrot-producing states. (USDA, National Ag Statistics Service, 2016).

Exclusive Use Data Protection Criteria Fluensulfone Satisfies:

Criterion (II) the alternatives to the minor use pesticide pose greater risks to human health:

In this minor use crop the fluensulfone product Nimitz can replace the commercial use of Vapam HL (i.e. metham sodium), Telone C-17 (i.e. 1,3-dichloropropene + chloropicrin) and Telone II (i.e. 1,3-dichloropropene) all of which are restricted use fumigants requiring a site-specific management plan. Nimitz can also replace Vydate L and Vydate C-LV (i.e. oxamyl) which are carbamates with neurotoxic potential (See appendix 2).

- Vapam HL, Telone C-17, Telone II, Vydate L, and Vydate C-LV all have the potential to cause more harm to the environment and human health when compared Nimitz. Nimitz carries a “Caution” label, while Vepam HL, Telone C-17, Vydlate L, and Vydate C-LV carry a “Danger” label and Telone II carries a “Warning” label (Appendix 2) with the following human safety text included:

- Vepam HL: DANGER: Fatal if absorbed through skin. Corrosive. Causes skin burns and irreversible eye damage. Do not get in eyes, on skin or on clothing. May be fatal if swallowed or inhaled. Do not breathe vapors or spray mist. Prolonged or frequently repeated skin contact may cause allergic reactions in some individuals.

- Telone C-17: DANGER: May cause lung liver, and kidney damage and respiratory system irritation upon prolonged contact. The use of this product may be hazardous to your health. This product contains 1,3-dichloropropene, which has been determined to cause tumors in laboratory animals. Risks can be reduced by exactly following direction for use, precautionary statements, by wearing the personal protective equipment specified in this labeling. Fatal if inhaled or swallowed. Poisonous Liquid and vapor. Corrosive. Liquid causes skin burns and irreversible eye damage. Do not breathe vapor or gas. Do not get in eyes, on skin or on clothing. Chloropicrin is readily identifiable by smell. Exposures to very low concentrations of vapor will cause irritation of eyes, nose, and throat. Continued exposure after irritation occurs, or exposure to higher concentration may cause painful irritation or temporary blindness.

- Telone II: WARNING: Do not swallow any of this product. May be fatal if swallowed. Do not get in eyes. Causes substantial, but temporary eye injury. Do not get on skin. May be fatal if absorbed through the skin. Causes skin irritation and, if confined, skin burns. May cause allergic skin reaction. Do not breathe vapor. May be fatal if inhaled. May cause lung, liver, and kidney damage and respiratory system irritation upon prolonged contact. The use of this product may be hazardous to your health. This product contains 1,3-dichloropropene, which has been determined to cause tumors in laboratory animals. Risks can be reduced by exactly following direction for use, precautionary statements, by wearing the personal protective equipment specified in this labeling.

- Vydate L: DANGER: Fatal if swallowed. May be fatal if inhaled. Do not breathe spray mist. Causes moderate eye irritation. Avoid contact with eyes or clothing. Contains methanol which may cause blindness.

- Vydate C-LV: DANGER: Fatal if swallowed. Corrosive. Causes irreversible eye damage. May be fatal if inhaled. Do not breathe vapor. Do not get in eyes or on clothing. Wash hands before eating, drinking, chewing gum, using tobacco

All five formulations also require special personal protective equipment (PPE) (Appendix 4), and Vepam HL, Telone C-17 and Telone II require certified applicator training and licensing, and special posting. Additionally, in the case of Telone C-17 and Telone II both products also cannot be applied within 100 feet of an occupied structure.

The toxicological profile of metham sodium, 1,3-dichloropropene, chloropicrin, and oxamyl (Appendix 1), as well as the acute toxicity of Vapam HL, Telone C-17, Telone II, Vydate L, and Vydate C-LV (Appendix 2 and 3), shows that these actives and associated formulations present an increased toxic potential to humans when compared to fluensulfone and its formulated product Nimitiz.

Two other alternative products to Nimitz in this minor use crop are Velum One and Velum Prime (i.e. Fluopyram). While all three formulations present a largely similar risk to human health, with the exception of Nimitiz which is labeled as a skin sensitizer.

Velum One and Velum Prime presents a larger concern for the environment due to its high potential for groundwater contamination even after several months following application:

- Velum One & Prime: For terrestrial uses – Do not apply direct to water, or to areas where surface water is present or to intertidal areas below the mean high-water mark. Do not contaminate water when disposing of equipment wash water or rinsate. This product may impact surface water quality due to runoff of rain water. This is especially true for poorly draining soils and soil with shallow ground water. This product is classified as having a high potential for reaching surface water via runoff for several months or more after application. A level, well-maintained vegetative buffer strip between areas to which this product is applied and surface water features such as ponds, streams, and springs will reduce the potential loading of Fluopyram. Runoff of this product will be reduced by avoiding application when rainfall or irrigation is expected to occur within 48 hours. Sound erosion control practices will reduced this product's potential to reach aquatic sediment via runoff. This chemical has properties and characteristics associated with chemical detected in ground water. This chemical my leach into groundwater if used in areas where soils are permeable, particularly where the water table is shallow.

Based on the information presented above, it can thus be concluded that fluensulfone, formulated as Nimitz poses less risk to human health when compared to the alternative registered products: Vapam HL, Telone C-LV, Telone II, Vydate L, Vydate C-LV, Velum One, and Velum Prime.

Criterion (III) the minor use pesticide plays or will play a significant part in managing pest resistance:

The Agency in 2017 issued the PR-Notice 2017-01 that recommends rotating a pesticide with other chemicals with different modes of action over several applications, to avoid the genes responsible for the resistant trait can spread quickly through the population.

According to EPA (2018) "Pesticide resistance may occur when genetic or behavioral changes enable a portion of a plant pest populations (such as bacteria, fungi, insects or other organisms) to tolerate or survive what would otherwise be lethal doses of a pesticide. The surviving pest populations increase with continued exposure to a no longer effective pesticide. Resistance to pesticides by plant pest appears to be increasing in the U.S. and worldwide. Managing the evolution of pesticide resistance in plant pests is an important part of sustainable pest management and an integral part of IPM programs, to assist crop producers to manage plant pests effectively. The development of pesticide resistance is influenced by a number of factors. One important factor that fosters pesticide resistance is the repeated use of pesticides with the same mode of action on the same pest population. Repeated use of a pesticide with a single mode of action kills sensitive pests but allows pests in the population that are tolerant of the pesticide to increase in numbers. These individuals will generally be unaffected by the repeated pesticide applications and may ultimately make-up a substantial portion of the pest population. Thus, an important proactive pesticide resistance-management strategy is to rotate pesticides with different modes of action to increase the likelihood of controlling of target pests in any given location or area. This approach may delay and/or prevent the development of resistance to a particular mode of action without resorting to increased rates and frequency of application and may prolong the useful life of pesticides."

Due to the similar and or superior efficacy of fluensulfone to other nematicides, it is a valuable tool for rotation of different Mode of Action (MoA) Nematicide. See below the different Nematicide and its MOA.

Table 2: Registered Nematicides and MoA.

Nematicide Active Ingredient and Brand	MoA Description of MoA	Control
Fluensulfone (NIMITZ – EPA Reg. N.# 66222-243)	Fluoroalkenyl pleiotropic expression of activity against nematodes	Nematodes only
Oxamyl (Vydate – EPA Reg. N.# 352-372 and 352-532)	Carbamate inhibition of the enzyme AChE, which cleaves the neurotransmitter acetylcholine	Insects. Acara, Mites, Nematodes and Plant growth regulator
Fluopyram (Velum – EPA Reg. N.# 264-1078)	SDHi inhibition of succinate dehydrogenase in the respiration chain	Fungi and Nematodes
Metham Sodium (Vapam HL– EPA Reg. N.# 5481-468)	Methylcarbamate inhibition of the enzyme AChE, which cleaves the neurotransmitter acetylcholine	Fungi, Insects and Nematodes
1,3-D (Telone C-17 and Telone II – EPA Reg. N.# 62719-12 and 62719-32)	Halohydantoins reacts with an unidentified vital enzyme system (or systems) at a site on the enzyme containing sulfhydryl (sulfur + hydrogen), ammonia, or hydroxyl (oxygen + hydrogen) ions	Fungi, Insects and Nematodes
Chloropicrin (Telone C-17 – EPA Reg. N.# 62719-12)	Fumigants Several complex biochemistry reactions	Fungi, Insects and Nematodes

Criterion (IV): the minor use pesticide plays or will play a significant part in an integrated pest management program.

Fluensulfone is a pyrazole nematicide and is the first nematicide in the fluoroalkenyl class (Phillion et al., 1999; Oka et al., 2008; Oka et al., 2009). It targets Root-knot (*Meloidogyne* spp.), Potato cyst (*Globodera* spp.), Needle (*Longidorus africanus*), Lance (*Hoplolaimus* spp.), Sting (*Belonolaimus* spp.), stubby root (*Trichodorus* and *Paratrichodorus* spp.), and Lesion (*Pratylenchus* spp.). Because of its unique mode-of-action, Fluensulfone can break a cycle of pest resistance developing in the field and assist in managing pest resistance with an alternate chemistry to product currently registered.

ADAMA sponsored field trials in Florida and California to obtain efficacy and plant safety data to support the use of Nimitz in Crop Group1. Root and Tuber Vegetables, Subgroup 1B, Root Vegetables (except Sugar Beets) with trials in Carrots production. The following summary will support the use in Carrot and Radish Production.

Table 3: Summary of Efficacy Studies with Nimitz Nematicide on Carrots

Exhibit No. - Year	Cooperator Affiliation Test Location	Crop Planting Method	Nematode	Nimitz Rates (Fl Oz/A) [Pints/A]	Application Method Standard(s)	Overview of Results
2009	Dr. Don W. Dickson, University of Florida, Gainesville, FL	Carrot Seed	Root-knot	[1.7, 3.4, 5.1, 6.8]	Vydate 2L 6.0 lb ai/ac	No phyto. reported; tested as Nimitz 480EC; Number of taproots was higher in all treated plots than in the nontreated control plots except for MCW-2 at 5.1 pts/A; Total and marketable yields were significantly higher in all treated plots than in the nontreated control.; high percentage yield loss of 46% between total yield and marketable yield in the nontreated plots.
2010	Dr. B. Westerdahl UC Davis Irvine, CA	Carrot Seed	Root-knot	[3.5, 5, 7]	Banded, (12”), PPI Telone	No phyto. reported; tested as MCW-2; root gall ratings with all Nimitz rates significantly lower than UTC but = to Telone; at harvest Nimitz had significant increase in marketable carrots =Telone.
2015	Dr. Ole Becker UC Riverside Irvine, CA	Carrot Seed	Root-knot	[5, 7]	Banded, (20”), PPI	No phyto. reported; Tested as Nimitz 480 EC; root galling significantly lower in

						both Nimitz treatments compared to UTC; Nimitz treatments provided significant yield increases; Nimitz showed significant protective activity under high RKN pressure.
2015	Dr. B. Westerdahl UC Davis Irvine, CA	Carrot Seed	Root-knot	[3.5, 5, 7]	Banded (12”) PPI Vydate	No phyto. reported; tested as Nimitz 480EC; RKN significantly reduced with 5 and 7 pt/a rates; numerical reduction compared to UTC with 3.5 pt/a rate; numerically higher marketable carrots in Nimitz treatments compared to UTC.
2016	John Ojala and Sherod Craig Sun Pacific Poplar & Earlimart, CA	Establish ed Kiwifruit Vines	Root-knot	[4 and 5.6 in split apps. of 2, 2.8]	Banded over berm; sprinkler irrigation incorporati on	No phyto. reported; tested as Nimitz; Due to variability in RKN counts, data from Trial 1 and Trial 2 were combined; RKN population was significantly less in plots treated with Nimitz at 5.6 pt/a; 95% control of population between May and July and 75% control between July and September.

Testimonial Letters support the use of fluensulfone in carrots pointed out the importance of the product in the control of nematodes:

1. In testimonial letter from University of California (dated December 9, 2019, Testimonial 1), the Vegetable /Plant Pathology Advisor from University of California Cooperative Extension pointed out the benefit of Fluensulfone for carrots. He points out that Fluensulfone “offers increased opportunity for integrated approaches to be used for both pest and soil nutrient management programs when compared to other currently registered alternatives. This new nematicide product is selective for nematodes relative to older chemistries such as fumigants and oxamyl, which will allow growers increase flexibility in using them and opportunities for increase soil nutrient management and integrated pest management techniques to be practiced”. According to this researcher, Fluensulfone increases “growers capacity to practice field management strategies that better promote beneficial bacteria, earthworms, and insect populations contributing to strong IPMA programs and more sustainability stewardship practices.”

2. In similar analysis, Becky B. Westerdahl from University of California Cooperative Extension Specialist in nematology also pointed out that fluensulfone can be a valuable tool to use in the IPM grower program (Testimonial 2).

3. University of Michigan has also tested the product for carrots and found this tool to be valuable for carrots (Testimonial 3). A crisis exemption was issued on 14 April 2015 was issued by the Michigan Department of Agriculture for the use of fluensulfone to control a number of nematode species in carrot fields. This was the first Section 18 exemption for this use. Under the exemption, up to 2,000 acres of carrot fields will be treated with the Nimitz® formulation of fluensulfone (EPA Registration No. 66222-243). The use season is 14 April to 15 June 2015.

The EPA granted to the Michigan Department of Agriculture a crisis exemption for the use of fluensulfone to control a number of nematode species in carrot fields. This was the first Section 18 exemption for this use. Under the exemption, up to 2,000 acres of carrot fields will be treated with the Nimitz. The Section 18 documentation indicates that the use will be in counties of Lapeer, Montcalm, Newaygo, and Oceana. The use season is 14 April to 15 June 2015, and the crisis exemption was issued on 14 April 2015. (Appendix 4).

Conclusion

Fluensulfone provides carrot growers with an effective tool to combat problematic species of root knot nematode (*Meloidogyne* spp.), lesion nematode (*Pratylenchus* spp.), stubby-root nematode (*Trichodorus* spp.) as well as Potato cyst (*Globodera* spp.), Needle (*Longidorus africanus*), Lance (*Hoplolaimus* spp.), Sting (*Belonolaimus* spp.), and *Paratrichodorus* spp.). Fluensulfone satisfies EPA’s criteria:

II: Fluensulfone is an alternative to the minor use pesticide pose greater risks to human health with a softer toxicological profile in comparison to most current pesticides currently registered in the US, decreasing risk of occupational exposure;

III: Fluensulfone will play a significant part in managing pest resistance as a novel MoA against specific nematodes; while keeping a softer effect on other beneficial soil communities;

IV: Fluensulfone will play a significant part of integrated pest management plan as easier to use tool and price competitive in comparison to current fumigant and oxamyl options.

b. Sweet Potato

Sweet potatoes are a tropical, long season vegetables that grow best in long hot summers where they can get at least 150 frost-free days. Due to their growing requirements, sweet potatoes are primarily grown on a large commercial scale in the southern United States. Since 1971, North Carolina is the leading sweet potato production state, producing approximately 60 percent of all sweet potatoes grown in the country.

U.S. sweet potato production has increased substantially over the last 15 years. National production increased by an average of 6.1 percent per season since 2000, with a record high production of 31.54 million hundredweight in 2016 with an estimated value of $705.69 million. The increase in sweet potato production is due, in part, to an increase in acreage harvested from 95,000 acres in 2000 to 163,300 acres in 2016 (USDA ERS, 2016)

Exclusive Use Data Protection Criteria Fluensulfone Satisfies:

Criterion (II) the alternatives to the minor use pesticide pose greater risks to human health:

Please see section 5.a. for information on the alternative registered products for sweet potato and the risk they pose to the environment and human health when compared to fluensulfone formulated as Fluensulfone 480 EC.

Criterion (III) the minor use pesticide plays or will play a significant part in managing pest resistance:

Please see section 5.a. for information on the alternative registered products for sweet potato and role that fluensulfone plays in managing pest resistance.

Criterion (IV): the minor use pesticide plays or will play a significant part in an integrated pest management program.

ADAMA sponsored field trials in California and Washington to obtain efficacy and plant safety data to support the use of Nimitz in sweet potato production.

Table 4 - Summary of Efficacy Studies with Nimitz Nematicide to Support Use in Sweet Potato

Exhibit No. - Year	Cooperator Affiliation Test Location	Crop Planting Method	Nematode	Nimitz Rates (Fl Oz/A) [Pints/A]	Application Method Standard(s)	Overview of Results
2015	Antoon Ploeg UC Riverside Irvine, CA	Sweet Potato Slips	Root-knot	[6]	38" band over beds, PPI Vapam	**No phyto. reported**; tested as Nimitz; Significant total yield increase with Nimitz as well as significant marketable yield increase with Nimitz; Significant decrease in RKN infested sweet potatoes; significant decrease in RKN eggs in sweet potato roots.
2016	Antoon Ploeg UC Riverside Irvine, CA	Sweet Potato Slips	Root-knot (*M. incognita*)	[6]	38" band over beds, PPI Vapam	**No phyto. reported**; tested as Nimitz; At 3.5 pt/acre or 5.0 pt/acre, Nimitz applied as an incoporated soil drench 7 days prior to planting nematode-susceptible sweetpotato infested soil, increased total root yield by about 30%, doubled the marketable yield, and reduced nematode infestation of sweetpotato roots by over 85% compared to a non-treated control. There are no indications that increasing the Nimitz rate from 3.5 to 5.0 pt/acre provided any additional benefit. Nimitz did not reduce soil RKN levels at harvest time (Pf), and did not affect the number of sweetpotato roots that were harvested
Overall 2015 & 2016 Trials: The results from field trials with Nimitz on sweetpotato grown on root-knot nematode infested soil were very similar in 2015 and 2016. The general set-up of the trial and nematode species (*M. incognita*) was the same, but the sweetpotato cultivar grown was different (O'Henry in 2015, Beauregard in 2016). In both years, pre-plant soil-incorporated applications of Nimitz significantly						

<table>
<tr><td colspan="7">increased total yields (2-fold in 2015, 1.3-fold in 2016), and percentage marketable yields (5-fold in 2015, 2-fold in 2016). Furthermore, Nimitz treatments dramatically reduced the nematode load of the harvested roots in both years by over 80%. In both years, Nimitz treatments did not reduce the root-knot nematode levels in the soil at harvest time. The effect on the total number of roots harvested per plot were different between the two years: in 2015 Nimitz increased the number of roots from 85 in the untreated control to 125, whereas in 2016 about 90 roots were harvested from Nimitz and untreated control plots. This may be due to differences in tolerance between the sweetpotato cultivars that were used in 2015 and 2016.</td></tr>
<tr><td>2016-2017</td><td>Adama Internal Trial</td><td>Sweet Potato Slips</td><td>Root-knot</td><td>[3.5, 4.9, 6.0]</td><td>Metam-sodium 251 pts/A</td><td>No phyto. reported; tested as MCW 480 SC; although Nimitz did not reduce soil nematode levels at harvest, a PPI drench of 3.5 pts/A could be a valuable alternative for currently used nematicides to mitigate root know nematode damage. In 2016, yield was significantly higher than UTC and in 2017 Nimitz proved 9 kg/plot more yield than UTC.</td></tr>
</table>

In a publication of the Journal of Nematology (Ploeg et al 2019), fluesnulfone treatments more than doubled the marketable yields over an untreated control and a metam-sodium treatment in trials to control Root-knot (*Meloidogyne* spp). (Appendix 5)

According to Kawanobe et al (2019), the use of nematicides with reduced toxic side-effects against non-target free-living nematodes is a favorable option for farmers to control plant-parasitic nematodes. A study was conducted to evaluate the nematicidal activity of fluensulfone against non-target nematode fauna in four field experiments, each under different conditions (soils types and plant hosts). Nematodes extracted from soil samples were classified and counted based on their morphological characters. Fluensulfone significantly reduced damage caused by root-knot nematodes to sweet potato plants, while overall non-target free-living nematode population densities were maintained at the same level as those in control. Four experiments showed that fluensulfone treatment kept a similar diversity level of non-target free-living nematode fauna to that of the non-treated control. The results suggested that fluensulfone may have minimal impact to free-living nematode fauna in both population density and diversity when the nematicide was applied to control *Meloidogyne* spp. (Appendix 6)

According to EPA (2018), there are few nematicides options available to control nematodes on sweet potatoes, fluensulfone is one the most recent registrations that are allowed to use against emergent nematode pest such as *Meloidogyne enterolobii*.

Conclusion

Fluensulfone provides sweet potatoes growers with an effective tool to combat problematic species of root knot nematode (Meloidogyne spp.), lesion nematode (*Pratylenchus* spp.), stubby-root nematode (*Trichodorus* spp.) as well as Potato cyst (*Globodera* spp.), Needle (*Longidorus africanus*), Lance (*Hoplolaimus* spp.), Sting (*Belonolaimus* spp.), and *Paratrichodorus* spp.). Fluensulfone satisfies EPA's criteria:

II: Fluensulfone is an alternative to the minor use pesticide pose greater risks to human health with a softer toxicological profile in comparison to most current pesticides currently registered in the US, decreasing risk of occupational exposure;

III: Fluensulfone will play a significant part in managing pest resistance as a novel MoA against specific nematodes; while keeping a softer effect on other beneficial soil communities;

IV: Fluensulfone will play a significant part of integrated pest management plan as easier to use tool and price competitive in comparison to current fumigant and oxamyl options.

c. Okra

Okra is such a small crop, A reliable source of information for total acreage in the US is not available.

Exclusive Use Data Protection Criteria Fluensulfone Satisfies:

Criterion (II) the alternatives to the minor use pesticide pose greater risks to human health:

Please see section 5.a. for information on the alternative registered products for okra and the risk they pose to the environment and human health when compared to fluensulfone formulated as Fluensulfone 480 EC.

Criterion (III) the minor use pesticide plays or will play a significant part in managing pest resistance:

Please see section 5.a. for information on the alternative registered products for okra and role that fluensulfone plays in managing pest resistance.

Criterion (IV): the minor use pesticide plays or will play a significant part in an integrated pest management program.

ADAMA sponsored field trials in California and Washington to obtain efficacy and plant safety data to support the use of Nimitz in okra production.

Table 5: Summary of Efficacy Studies with Nimitz Nematicide to Support Use in Okra.

Exhibit No. - Year	**Cooperator Affiliation <u>Test Location</u>**	**Crop Planting Method**	**Nematode**	**Nimitz Rates (Fl Oz/A) [Pints/A]**	**Application Method Standard(s)**	**Overview of Results**
2014	G.E. Vallad, H. Adkison, R. Willis, and J. Siebert University of Florida, GCREC Wimauma, FL	Okra seeded	Root Knot, *Meloidogyne* spp	[2.1, 3.7]	Vydate 4.0 pt drip	**No phyto. recorded;** tested as Nimitz. Plant height and galling measurements were taken; Plant height was significantly different between the UTC and the 3.7 pt rate of Nimitz and Vydate; and galling was significantly for both Nimitz trts and Vydate compared to the UTC. Nimitz and Vydate were similar.
2008	Adama Internal Trial Dinuba, CA	Okra seeded	Root Knot, *Meloidogyne* spp	KG ai/A 1.0, 1.5, 2.0, 3.0, 4.0, 6.0, 1.5X2, 2.0+1.5, 3.0+1.5, 2.0X2, 3.0+2.0	Broadcast; Std Vydate 1.1 kg ai/A	**No recorded phyto.;** tested as MCW-2. UTC had the greatest root galling, but no significant differences or obvious numerical trends among treatments of MCW-2. However, all MCW-2 treatments had numerically lower root infections compared to the standard, Vydate.

Conclusion

Fluensulfone provides okra producers with an effective tool to combat problematic species of root knot nematode (*Meloidogyne* spp.), lesion nematode (*Pratylenchus* spp.), stubby-root nematode (*Trichodorus* spp.) as well as Potato cyst (*Globodera* spp.), Needle (*Longidorus africanus)*, Lance (*Hoplolaimus* spp.), Sting (*Belonolaimus* spp.), and *Paratrichodorus* spp.). Fluensulfone satisfies EPA's criteria:

II: Fluensulfone is an alternative to the minor use pesticide pose greater risks to human health with a softer toxicological profile in comparison to most current pesticides currently registered in the US, decreasing risk of occupational exposure;

III: Fluensulfone will play a significant part in managing pest resistance as a novel MoA against specific nematodes; while keeping a softer effect on other beneficial soil communities;

IV: Fluensulfone will play a significant part of integrated pest management plan as easier to use tool and price competitive in comparison to current fumigant and oxamyl options.

d. Pepper, bell

Bell peppers are widely grown all over the United States. The majority of bell peppers are produced in the open field on raised beds using drip irrigation and mulch. The US total harvested bell pepper acreage decreased from 62,080 acres in 2000 to 40,900 acres in 2015. California, Florida, and Georgia are the three largest bell-pepper-producing US states. Bell pepper acreage in Florida has shown a prominent declining trend due to increased market competition from Mexico and the phase-out of methyl bromide soil fumigant. The harvested acreage in Florida declined from 18,400 acres in 2000 to 12,200 acres in 2015. California's harvested acreage declined from 21,000 acres in 2000 to 19,500 acres in 2015. The harvested acreage in Georgia remained relatively stable between 2000 and 2015.
(Trina Biswas, Zhengfei Guan, and Feng Wuhttps://edis.ifas.ufl.edu/fe1028)

Exclusive Use Data Protection Criteria Fluensulfone Satisfies:

Criterion (II) the alternatives to the minor use pesticide pose greater risks to human health:

Please see section 5.a. for information on the alternative registered products for bell peppers and the risk they pose to the environment and human health when compared to fluensulfone formulated as Fluensulfone 480 EC.

Criterion (III) the minor use pesticide plays or will play a significant part in managing pest resistance:

Please see section 5.a for information on the alternative registered products for bell peppers and role that fluensulfone plays in managing pest resistance.

Criterion (IV): the minor use pesticide plays or will play a significant part in an integrated pest management program.

ADAMA sponsored field trials in California and Washington to obtain efficacy and plant safety data to support the use of Nimitz in Bell Pepper production.

Table 6: Summary of Efficacy Studies with Nimitz Nematicide to Support Use in Bell Pepper.

Exhibit No. - Year	Cooperator Affiliation Test Location	Crop Planting Method	Nematode	Nimitz Rates (Fl Oz/A) [Pints/A]	Application Method Standard(s)	Overview of Results
2014	Adama Internal Trial Immokalee, FL	Bell Peppers, Transplant	Root Knot, *Meloidogyne* spp	[3.5, 5.0]	Drip; Field treated with Chloropicri n and then Follow-by with Nimitz	**No phyto. recorded;** tested as Nimitz. NIMITZ at the 5 pt/acre rate reduced root galling and numbers of plant parasitic nematodes (*Meloidogyne sp.*) significantly compared to Chloropicrin alone on peppers.
2012	Pacific Ag Arroyo Grande, CA	Bell Peppers, Transplant	Root Knot, *Meloidogyne* spp	KG ai/A 2.0, 3.0, 4.0	Injection or drip; Std Vydate 4,6,8 pt/a; Telon 12 gal/a	**No recorded phyto.;** tested as MCW-2. Root galling was reduced at both evaluation dates from all rates of MCW-2 480 EC; All MCW-2 480 EC treatments significantly reduced galling severity at 159 DAA up to 97%, a positive rate response was observed to 3 kg ai/ha, and all rates were comparable to the three commercial standards; Among experimental treatments, MCW-2 at 2 kg ai/ha had a greater total yield at 32,417 lbs of peppers/acre

Testimonial Letter for the Use of Fluensulfone in Peppers:

Wilbur Ellis Company tested fluensulfone (Testimony Letter 4) against problematic species of root-knot (*Meloidogyne* spp.) and stubby-root nematodes (*Trichodorus* spp.) on bell peppers with a control of 70% with an increase yield. As mentioned in Testimonial 2 from University of California at Davis, Wilbur Ellis Company also considers fluensulfone a valuable alternative nematicide for fumigants and oxamyl.

Conclusion

Fluensulfone provides bell pepper producers with an effective tool to combat problematic species of root knot nematode (*Meloidogyne* spp.), lesion nematode (*Pratylenchus* spp.), stubby-root nematode (*Trichodorus* spp.) as well as Potato cyst (*Globodera* spp.), Needle (*Longidorus africanus)*, Lance (*Hoplolaimus* spp.), Sting (*Belonolaimus* spp.), and *Paratrichodorus* spp.). Fluensulfone satisfies EPA's criteria:

II: Fluensulfone is an alternative to the minor use pesticide pose greater risks to human health with a softer toxicological profile in comparison to most current pesticides currently registered in the US, decreasing risk of occupational exposure;

III: Fluensulfone will play a significant part in managing pest resistance as a novel MoA against specific nematodes; while keeping a softer effect on other beneficial soil communities;

IV: Fluensulfone will play a significant part of integrated pest management plan as easier to use tool and price competitive in comparison to current fumigant options.

e. Watermelon

According to the USDA Economic Research Service, over 113.000 acres of watermelons were grown in the US in 2017, producing approximately 40 million pounds. Most of the production occurs in four states – Texas, Florida, Georgia, and California. U.S. Cash receipts for watermelons was $578.8million in 2016. (USDA ERS 2017).

Exclusive Use Data Protection Criteria Fluensulfone Satisfies:

Criterion (II) the alternatives to the minor use pesticide pose greater risks to human health:

Please see section 5.a for information on the alternative registered products for watermelon and the risk they pose to the environment and human health when compared to fluensulfone formulated as Fluensulfone 480 EC.

Criterion (III) the minor use pesticide plays or will play a significant part in managing pest resistance:

Please see section 5.a for information on the alternative registered products for watermelon and role that fluensulfone plays in managing pest resistance.

Criterion (IV): the minor use pesticide plays or will play a significant part in an integrated pest management program.

ADAMA sponsored a field trial in Florida to obtain efficacy and plant safety data to support the use of Nimitz on watermelon. In spring 2014, experimental plots were established at a grower cooperator site in Wimauma, FL to assess the benefits of Nimitz for managing root-knot nematodes in double-cropped watermelon production along with a grower Vydate program (standard treatment) and an untreated control. On 14 Mar, plots were sampled for total nematode counts consisting of 4 composite soil samples derived from 20 separate 100 cc soil cores pulled from 4 separate 20 foot sampling areas along each plot. Watermelon vigor was determined on 16 Apr by measuring vine lengths and root galling was measured on, with 0 having no symptoms of root-knot galling and 10 having solid galling with no visible roots. Nimitz treatment had significantly less galls than the Vydate treatment and the untreated control at the first evaluation on March 28 demonstrating that Nimitz can used to control root-knot nematode; *Meloidogyne incognita*.

Table 7. Summary of Efficacy Studies with Nimitz Nematicide to Support Use in Watermelon.

Exhibit No. - Year	**Cooperator Affiliation <u>Test Location</u>**	**Crop Planting Method**	**Nematode**	**Nimitz Rates (Fl Oz/A) [Pints/A]**	**Application Method Standard(s)**	**Overview of Results**
2014	G.E. Vallad, H. Adkison, R. Willis, J. Siebert, S. Newman, S. Kalb, and B.S. Hughes Gulf Coast Research and Education Center University of Florida, GCREC Wimauma, FL 33598	Watermelon (*Citrullus lanatus var. lanatus*)	root-knot nematode *Meloidogyne incognita.*	(84, 112) [5, 7]	Injection into Drip Irrigation	**No phyto.;** No differences in vine length between treatments but significantly less galling with Nimitz on the first evaluation; by end of trial approx. 2 months later all treatments had similar galling.

Support Letters for the Use of Fluensulfone in Watermelons:

In the testimonial letter from The University of Florida (dated December 16, 2019, Testimonial 5), the assistant Professor Nematology, Johan Desaeger pointed out that this product provides "a new and safer tool to combat problematic nematode species, especially root-knot nematodes, the most problematic nematodes in Florida." The researcher also points out that this new tool can be a replacement for older chemistries such as fumigants and oxamyl.

In addition to that, recent scientific publication (Kawanobe, M. et all, 2019) pointed out that fluensulfone may serve well for maintaining a diverse free-living nematode community while suppressing root-knot nematodes.

Conclusion

Fluensulfone provides watermelon producers with an effective tool to combat problematic species of root knot nematode (*Meloidogyne* spp.), lesion nematode (*Pratylenchus* spp.), stubby-root nematode (*Trichodorus* spp.) as well as Potato cyst (*Globodera* spp.), Needle (*Longidorus africanus)*, Lance (*Hoplolaimus* spp.), Sting (*Belonolaimus* spp.), and *Paratrichodorus* spp.). Fluensulfone satisfies EPA's criteria:

II: Fluensulfone is an alternative to the minor use pesticide pose greater risks to human health with a softer toxicological profile in comparison to most current pesticides currently registered in the US, decreasing risk of occupational exposure;

III: Fluensulfone will play a significant part in managing pest resistance as a novel MoA against specific nematodes; while keeping a softer effect on other beneficial soil communities;

IV: Fluensulfone will play a significant part of integrated pest management plan as easier to use tool and price competitive in comparison to current fumigant and oxamyl options.

f. Cantaloupe

Melons belong to the Cucurbit family, which include cantaloupes. Cucurbits are thought to have originated in southern Mexico and Central America. Today's predominant melon varieties include watermelon, cantaloupe and honeydew. The U.S. cantaloupe acreage decreased from 66,350 acres in 2012 to 51,600 acres in 2015. (Ag Marketing Resource Center 2018).

Exclusive Use Data Protection Criteria Fluensulfone Satisfies:

Criterion (II) the alternatives to the minor use pesticide pose greater risks to human health:

Please see section 5.a. for information on the alternative registered products for cataloupe and the risk they pose to the environment and human health when compared to fluensulfone formulated as Fluensulfone 480 EC.

Criterion (III) the minor use pesticide plays or will play a significant part in managing pest resistance:

Please see section 5.a. for information on the alternative registered products for cataloupe and role that fluensulfone plays in managing pest resistance.

Criterion (IV): the minor use pesticide plays or will play a significant part in an integrated pest management program.

ADAMA sponsored field trials in California and Washington to obtain efficacy and plant safety data to support the use of Nimitz in cantaloupe production.

Table 8 - Summary of Efficacy Studies with Nimitz Nematicide to Support Use in Cantaloupe.

Exhibit No. - Year	Cooperator Affiliation Test Location	Crop Planting Method	Nematode	Nimitz Rates (Fl Oz/A) [Pints/A]	Application Method Standard(s)	Overview of Results
2009	Agricultural Development Group Eltopia, WA	Cantaloupe Transplant	Northern & Columbia Root Knot	[1.7, 3.4, 5.1, 6.8]	Broadcast, PPI Vydate 1 gal/A; Vydate 1.5 gal drip	**No phyto.;** tested as MCW. No significant difference in nematode number, although Vydate treatments had less; Nimitz provided better root quality in Northern Root Knot trials than the UTC or the standard Vydate. but not statistically.
2009	Becker UC of Riverside Riverside, CA Fall 2009 (3254009-4)	Cantaloupe Seeded	Root-knot & others	[1.7, 3.4, 5.1, 6.8]	Broadcast, PPI Vydate 1 gal/A; Avicta seed treatment	**Some phyto.;** tested as MCW 480 SC. With increasing rate, saw less plant stand and weight in Nimitz plots; less root galling with Nimitz comparable to Vydate; all trts less than UTC.
2009	Adama Internal Trial	Cantaloupe Seeded	Northern Root-knot	Kg ai/A [0.96, 1.92, 2.88, 3.84	Broadcast, PPI Vydate	**No phyto. reported**; tested as MCW 480 SC; no significant difference in parameters measured except root quality at 153 days after planting; Nimitz treatments and Vydate were comparable and better than UTC.

Please see previous section for the analysis of the amount of active ingredients used in cantaloupe in the US

Testimonial Letters Supporting the Use of Nimitz in Cantaloupe Production

In the testimonial letter from The University of Florida (dated December 16, 2019, Testimonial 5), the assistant Professor Nematology, Johan Desaeger pointed out that this product provides “a new and safer tool to combat problematic nematode species, especially root-knot nematodes, the most problematic nematodes in Florida.” The researcher also points out that this new tool can be a replacement for older chemistries such as fumigants and oxamyl.

Testimonial 6 from Loom Farms also points out the benefits of Fluensulfone for cantaloupe growers.

Conclusion

Fluensulfone provides cataloupe producers with an effective tool to combat problematic species of root knot nematode (*Meloidogyne* spp.), lesion nematode (*Pratylenchus* spp.), stubby-root nematode (*Trichodorus* spp.) as well as Potato cyst (*Globodera* spp.), Needle (*Longidorus africanus)*, Lance (*Hoplolaimus* spp.), Sting (*Belonolaimus* spp.), and *Paratrichodorus* spp.). Fluensulfone satisfies EPA's criteria:

II: Fluensulfone is an alternative to the minor use pesticide pose greater risks to human health with a softer toxicological profile in comparison to most current pesticides currently registered in the US, decreasing risk of occupational exposure;

III: Fluensulfone will play a significant part in managing pest resistance as a novel MoA against specific nematodes; while keeping a softer effect on other beneficial soil communities;

IV: Fluensulfone will play a significant part of integrated pest management plan as easier to use tool and price competitive in comparison to current fumigant and oxamyl options.

g. Cherry

United States sweet cherry production in 2016 totaled 350,240 tons valued at $788 million. Washington led the nation in sweet cherry production (210,550 tons), followed by Oregon (62,080 tons) and California (55,000 tons) (USDA NASS 2017). In 2004 there were 78,275 bearing acres that increased slightly to 80,600 by 2006 (USDA NASS 2006).

Exclusive Use Data Protection Criteria Fluensulfone Satisfies:

Criterion (II) the alternatives to the minor use pesticide pose greater risks to human health:

Please see section 5.a for information on the alternative registered products for cherry and the risk they pose to the environment and human health when compared to fluensulfone formulated as Fluensulfone 480 EC.

Criterion (III) the minor use pesticide plays or will play a significant part in managing pest resistance:

Please see section 5.a for information on the alternative registered products for cherry and role that fluensulfone plays in managing pest resistance.

Criterion (IV): the minor use pesticide plays or will play a significant part in an integrated pest management program.

ADAMA sponsored field trials in California and Georgia to obtain efficacy and plant safety data to support the use of Nimitz in Cherry production.

Table 9: Summary of Efficacy Studies with Nimitz Nematicide to Support Use in Cherry Crops

Exhibit No. - Year	Cooperator Affiliation Test Location	Crop Planting Method	Nematode	Nimitz Rates (Fl Oz/A) [Pints/A]	Application Method Standard(s)	Overview of Results
2009	Adama Internal Field Trial Kelowna BC	Cherry Trees in field	Root lesion – *Pratylenchus* sp. Ring – *Circonemella* sp. Pin – *Pratylenchus* sp. Dagger – *Xiphinema* sp.	Trees were drenched with 2 litres of a 2000 ppm solution of product.	None	**No phyto. reported**; Tested as Experimental Product. The product reduced nematode levels. Root development was not inhibited and root tip dieback was reduced up to 55 days post application. The product had residual for up to 30 days, which suggests the application timing should be early spring just prior to root push. There were indications that the treatment controlled June bug larvae.
2017	Tracy Miller Linden, CA	Cherry, sweet	Lesion	[3.5, 5.0, and 7.0 pt/A]	Movento [9 fl oz/A]	**No phyto. reported;** Nimitz at 3.5 pt/A gave the greatest vegetative growth. All nematicide treatments gave significantly better control than the Untreated. Nimitz at 5 and 7 pt/A had significant fewer lesion nematodes than the Untreated.

Conclusion

Fluensulfone provides cherry producers with an effective tool to combat problematic species of root knot nematode (*Meloidogyne* spp.), lesion nematode (*Pratylenchus* spp.), stubby-root nematode (*Trichodorus* spp.) as well as Potato cyst (*Globodera* spp.), Needle (*Longidorus africanus)*, Lance (*Hoplolaimus* spp.), Sting (*Belonolaimus* spp.), and *Paratrichodorus* spp.). Fluensulfone satisfies EPA's criteria:

II: Fluensulfone is an alternative to the minor use pesticide pose greater risks to human health with a softer toxicological profile in comparison to most current pesticides currently registered in the US, decreasing risk of occupational exposure;

III: Fluensulfone will play a significant part in managing pest resistance as a novel MoA against specific nematodes; while keeping a softer effect on other beneficial soil communities;

IV: Fluensulfone will play a significant part of integrated pest management plan as easier to use tool and price competitive in comparison to current fumigant options.

h. Peach

As of 2017, peaches are commercially produced in 20 states. The top four states in peach production are California, South Carolina, Georgia and New Jersey.

In 2017, California supplied nearly 56 percent of the United States fresh peach crop and more than 96 percent of processed peaches (USAD NASS, 2018).

United States total peach production in 2017 was 690,100 tons valued at $599 million. California led the nation in peach production, with 541,000 tons valued at $376.5 million. New Jersey followed, producing 28,200 tons valued at $44 million. Pennsylvania produced 21,400 tons valued at $25.3 million, and Washington produced 12,770 tons valued at $12.3 million (USDA NASS, 2018).

The bearing acreage of peach trees has been gradually declining for the past two decades. By 2017 the United States had 92,750 bearing acres of peach trees. The value of production, however, has been gradually increasing over the past two decades (NASS 2018).

Exclusive Use Data Protection Criteria Fluensulfone Satisfies:

Criterion (II) the alternatives to the minor use pesticide pose greater risks to human health:

Please see section 5.a for information on the alternative registered products for peach and the risk they pose to the environment and human health when compared to fluensulfone formulated as Fluensulfone 480 EC.

Criterion (III) the minor use pesticide plays or will play a significant part in managing pest resistance:

Please see section 5.a for information on the alternative registered products for peach and role that fluensulfone plays in managing pest resistance.

Criterion (IV): the minor use pesticide plays or will play a significant part in an integrated pest management program.

ADAMA sponsored field trials in California and Georgia to obtain efficacy and plant safety data to support the use of Nimitz in Peach production.

Table 10. Summary of Efficacy Studies with Nimitz Nematicide to Support Use in Peach Crops

Exhibit No. - Year	Cooperator Affiliation <u>Test Location</u>	Crop Planting Method	Nematode	Nimitz Rates (Fl Oz/A) [Pints/A]	Application Method Standard(s)	Overview of Results
2016	James Noe Athens, GA	Peach, potted Greenhouse	Ring *Mesocriconema xenoplax*	[3.5, 7.0]	None	**No phyto. reported**; Tested as Nimitz. Significantly less nematodes inpots treated with Nimitz than UTC.
2018	James Noe and Ted Holladay Athens, GA	Peach Greenhosue and Field	Ring *Mesocriconema xenoplax* Root Knot *M. incognito*	[3.5 X 2, 30-day interval]	None	**No phyto. reported;** Nematode counts at 60, 90 and 120 days after application. Some evaluations were significantly less nematodes in Nimitz treatment and the trend was less nematodes in Nimitz treatments than UTC.
2018	Andrew M. Shirley et al Athens, GA	Peach, potted Greenhouse	Ring *Mesocriconema xenoplax* Root Knot *M. incognito*	(0.014 kg/ha)	None	**No phyto. reported**; Tested as Nimitz; At 40 DAI, Nimitz significantly reduced *M. incognita* numbers compared to the controls; no effect was seen at 70 DAI; At 30 DAI, Nimitz significantly reduced *M. xenoplax* numbers compared to the controls and was also efficacious against *M. xenoplax* 60 and 90 DAI.
2018	Brad Booker Parlier, CA	Peach, field (one-yr old)	lesion, ring and root-knot nematodes	[3.5, 5.0, and 7.0] X2	Velum One 6.84 fl oz/A	**No phyto. reported**; Tested as Nimitz ; No significant differences in crop vigor and trunk diameter were present among the treatments; At 139 DA-A, all Nimitz-treated plots (all rates) had significant fewer root-knot and ring nematodes than the Untreated. The was a similar trend for lesion nematode counts, but only Nimitz at 5 and 7 pt were significantly different than the Untreated. For all nematode counts, Nimitz at 7 pt was statistically similar to Velum One.

Conclusion

Fluensulfone provides peach producers with an effective tool to combat problematic species of root knot nematode (*Meloidogyne* spp.), lesion nematode (*Pratylenchus* spp.), stubby-root nematode (*Trichodorus* spp.) as well as Potato cyst (*Globodera* spp.), Needle (*Longidorus africanus)*, Lance (*Hoplolaimus* spp.), Sting (*Belonolaimus* spp.), and *Paratrichodorus* spp.). Fluensulfone satisfies EPA's criteria:

II: Fluensulfone is an alternative to the minor use pesticide pose greater risks to human health with a softer toxicological profile in comparison to most current pesticides currently registered in the US, decreasing risk of occupational exposure;

III: Fluensulfone will play a significant part in managing pest resistance as a novel MoA against specific nematodes; while keeping a softer effect on other beneficial soil communities;

IV: Fluensulfone will play a significant part of integrated pest management plan as easier to use tool and price competitive in comparison to current fumigant and oxamyl options.

i. Strawberry

In 2017, the United States harvested strawberries from 52,700 acres located in 10 states: 38,200 acres in California, 10,700 acres in Florida, and the remaining 3,800 acres from Oregon, North Carolina, Washington, New York, Michigan, Pennsylvania, Wisconsin, and Ohio (USDA NASS, 2017).

Average strawberry yield per acre was 50,500 pounds in 2017 and ranged from 68,000 pounds per acre in California to a low of 3,200 pounds per acre in New York (NASS, 2017). The large range between the yields per state is due to climate differences. California has a temperate climate, therefore allowing a 12-month growing season, and producing a higher yield per acre than other states. The climates of other states limit the growing season to an average of five-months, with some areas having a growing season as short as three weeks.

Exclusive Use Data Protection Criteria Fluensulfone Satisfies:

Criterion (II) the alternatives to the minor use pesticide pose greater risks to human health:

Please see section 5.a for information on the alternative registered products for strawberry and the risk they pose to the environment and human health when compared to fluensulfone formulated as Fluensulfone 480 EC.

Criterion (III) the minor use pesticide plays or will play a significant part in managing pest resistance:

Please see section 5.a for information on the alternative registered products for strawberry and role that fluensulfone plays in managing pest resistance.

Criterion (IV): the minor use pesticide plays or will play a significant part in an integrated pest management program.

ADAMA sponsored field trials in California and Florida to obtain efficacy and plant safety data to support the use of Nimitz on strawberries.

Table 11. Summary of Efficacy Studies with Nimitz Nematicide to Support Use on Strawberries.

Exhibit No. - Year	Cooperator Affiliation Test Location	Crop Planting Method	Nematode	Nimitz Rates (Fl Oz/A) [Pints/A]	Application Method Standard(s)	Overview of Results
2011	Dr. F. Sances Pacific Ag Research Guadalupe, CA	Strawberry Transplant	Root-knot & others	(84, 112) [5, 7]	Broadcast, PPI Methyl Bromide, Chlropicrin, Telone II	**No phyto.;** tested as MCW-2; no difference in plant growth; MCW-2 at 84 and 112 fl oz/a reduced rkn 94% = to standards.
2011-2012	Adama Internal Trial, Dover, FL – Florida Ag	Strawberry Transplant	Root-knot & others	[5.3, 7.1]	Broadcast fumigant Methyl Bromide, Chlropicrin or drip Telone II	**No phyto;** various combination of treatments; MB+Pic highest marketable yield but all trts had higher numerical yield than UTC; Nimitz + PIC controlled pest spectrum and produced a vigorous crop compared to UTC.
2015	Dr. B. Westerdahl UC Davis Irvine, CA	Strawberry Transplant	Root-knot	[3.5, 5]	Banded (12") PPI, Broadcast PPI, Drip, Telone	**No phyto. reported**; tested as Nimitz; no significant difference in terms of plant responses or gall ratings; Nimitz treatments and Telone reduced the root gall rating 57-71% lower than UTC; at harvest Nimitz treatments had numerically fewer RKN juveniles in the soil.
2016-17	David Holden Holden Research and Consulting Ventura, CA	Strawberry Transplant	Stubby Root	[3.5, 5, 7]	Drip, Chloropicrin	**No phyto. observed**; tested as Nimitz; stubby root nematode in all plots; No significant plant growth responses; did get significant yield increase at 7 pts/a Nimitz compared to UTC; Nimitz was similar to chloropicrin.
2015-16	J.W. Noling Univ. Florida Lake Alfred, FL Dover, FL	Strawberry Transplant	Sting	[2.5, 3.5 fall; 2.5, 3.5 spring]	Drip, Telone	**No phyto. reported**; tested as Nimitz; Nimitz treatments provided significant foliage growth and decrease in dead plants compared to UTC;

						Sting nematode numbers significantly reduced at end of season with Nimitz treatments.
2015	Adama Internal Trial, Dover, FL – Florida Ag Research Enda Farm.	Strawberry Transplant	Sting	[480EC 7 /2X3.5; 230CS 15/2X7.5; 380EW 9/2X4.5]	Drip, Telone	**No phyto. reported;** tested new Nimitz formulations 480 EC, 230CS, 380 EW**;** split appl half-rate; No stat. diff. but plots with 2 appl of 480EC or 380EW more marketable fruit; Sting nematode counts did not decrease
2017	J.W. Noling Univ. Florida Lake Alfred, FL Dover, FL	Strawberry Transplant	Sting	[2.5, 2.5 fall; 3.5, 3.5 spring]	Drip, Telone	**No phyto. reported**; tested as Nimitz; Nimitz treatments provided significant relative yield increase compared to Telone and UTC. Nimitz applied at 2.5 + 2.5 pt/a provided a 41% and at 3.5 + 3.5 pt/a provided a 42% yield increase compared to Telone at 19% increase over UTC.

Testimonial Letters Supporting the Use of Nimitz in Strawberry Production

In the testimonial letter from The University of Florida (dated December 16, 2019, Testimonial 5), the assistant Professor Nematology, Johan Desaeger pointed out that this product provides “a new and safer tool to combat problematic nematode species, especially root-knot nematodes, the most problematic nematodes in Florida.” The researcher also points out that this new tool can be a replacement for older chemistries such as fumigants and oxamyl. Testimonial 2 also points out the benefits of Fluensulfone for strawberries growers.

Conclusion

Fluensulfone provides strawberry producers with an effective tool to combat problematic species of root knot nematode (*Meloidogyne* spp.), lesion nematode (*Pratylenchus* spp.), stubby-root nematode (*Trichodorus* spp.) as well as Potato cyst (*Globodera* spp.), Needle (*Longidorus africanus)*, Lance (*Hoplolaimus* spp.), Sting (*Belonolaimus* spp.), and *Paratrichodorus* spp.). Fluensulfone satisfies EPA’s criteria:

II: Fluensulfone is an alternative to the minor use pesticide pose greater risks to human health with a softer toxicological profile in comparison to most current pesticides currently registered in the US, decreasing risk of occupational exposure;

III: Fluensulfone will play a significant part in managing pest resistance as a novel MoA against specific nematodes; while keeping a softer effect on other beneficial soil communities;

IV: Fluensulfone will play a significant part of integrated pest management plan as easier to use tool and price competitive in comparison to current fumigant and oxamyl options.

j. Kiwifruit

Kiwifruit was an unknown crop several decades ago, but it has gained worldwide acceptance in the last decade. Now it is a major fruit crop with 170,000 acres planted in both hemispheres. The United States has about 7,200 acres planted, of which almost all is planted within California. (www.calharvest.com)

Exclusive Use Data Protection Criteria Fluensulfone Satisfies:

Criterion (II) the alternatives to the minor use pesticide pose greater risks to human health:

Please see section 5.a for information on the alternative registered products for kiwi and the risk they pose to the environment and human health when compared to fluensulfone formulated as Fluensulfone 480 EC.

Criterion (III) the minor use pesticide plays or will play a significant part in managing pest resistance:

Please see section 5.a for information on the alternative registered products for kiwi and role that fluensulfone plays in managing pest resistance.

Criterion (IV): the minor use pesticide plays or will play a significant part in an integrated pest management program.

ADAMA sponsored field trials in Florida and California to obtain efficacy and plant safety data to support the use of Nimitz in Kiwi production.

Table 12. Summary of Efficacy Studies with Nimitz Nematicide to Support Use on Kiwi.

Exhibit No. - Year	Cooperator Affiliation Test Location	Crop Planting Method	Nematode	Nimitz Rates (Fl Oz/A) [Pints/A]	Application Method Standard(s)	Overview of Results
1 – 2016	John Ojala and Sherod Craig Sun Pacific Poplar & Earlimart, CA	Established Kiwifruit Vines	Root-knot	[4 and 5.6 in split apps. of 2, 2.8]	Banded over berm; sprinkler irrigation incorporation	**No phyto. reported;** tested as Nimitz; Due to variability in RKN counts, data from Trial 1 and Trial 2 were combined; RKN population was significantly less in plots treated with Nimitz at 5.6 pt/a; 95% control of population between May and July and 75% control between July and September.

Testimonial Letters Supporting the Use of Nimitz in Kiwifruit Production

In the testimonial letter from Kiwi Administrative Council (Appendix 7) discusses Nimitz efficacy results in Kiwi trials and promotes the use of Nimitz as a replacement for older chemistries that are problematic in the environment.

Conclusion

Fluensulfone provides kiwi producers with an effective tool to combat problematic species of root knot nematode (*Meloidogyne* spp.), lesion nematode (*Pratylenchus* spp.), stubby-root nematode (*Trichodorus* spp.) as well as Potato cyst (*Globodera* spp.), Needle (*Longidorus africanus)*, Lance (*Hoplolaimus* spp.), Sting (*Belonolaimus* spp.), and *Paratrichodorus* spp.). Fluensulfone satisfies EPA's criteria:

II: Fluensulfone is an alternative to the minor use pesticide pose greater risks to human health with a softer toxicological profile in comparison to most current pesticides currently registered in the US, decreasing risk of occupational exposure;

III: Fluensulfone will play a significant part in managing pest resistance as a novel MoA against specific nematodes; while keeping a softer effect on other beneficial soil communities;

IV: Fluensulfone will play a significant part of integrated pest management plan as easier to use tool and price competitive in comparison to current fumigant and oxamyl options.

k. Pecan and Macadamia (tree nuts)

In the US there are approximately 155,678 acres with Georgia leading the nation in pecan production, followed by New Mexico, Texas, and Arizona. (USDA NASS, 2017).

From 2013 to 2014, the value of pecan production stayed relatively steady for Georgia, New Mexico and Arizona, whereas, Texas experienced a large increase in value of pecan production from $44.8 million in 2013 to $107.8 million in 2014.

Exclusive Use Data Protection Criteria Fluensulfone Satisfies:

Criterion (II) the alternatives to the minor use pesticide pose greater risks to human health:

Please see section 5.a for information on the alternative registered products for pecan and macadamia and the risk they pose to the environment and human health when compared to fluensulfone formulated as Fluensulfone 480 EC.

Criterion (III) the minor use pesticide plays or will play a significant part in managing pest resistance:

Please see section 5.a for information on the alternative registered products for pecan and macadamia and role that fluensulfone plays in managing pest resistance.

Criterion (IV): the minor use pesticide plays or will play a significant part in an integrated pest management program.

ADAMA sponsored field trials in California and Georgia to obtain efficacy and plant safety data to support the use of Nimitz in Tree Nut production. Efficacy was conducted with the crop representatives for this Crop Grouping: Almond and Pecan.

Table 13. Summary of Efficacy Studies with Nimitz Nematicide to Support Use in Tree Nut Crops

Exhibit No. - Year	Cooperator Affiliation Test Location	Crop Planting Method	Nematode	Nimitz Rates (Fl Oz/A) [Pints/A]	Application Method Standard(s)	Overview of Results
2018	Brad Bokker San Luis Obispo, CA	ALMOND Trees in field	Root-knot Spiral Lesion	[3.5, 5.0, 7.0] Soil Drip	Velum One [6.84} Foliar	**No phyto. reported**; tested as Nimitz; At 33 DA-B, Nimitz at 5 and 7 pt/TA provided a significant reduction in root-knot nematodes compared to the Untreated. By 90 DA-B, all Nimitz rates provided significant nematode control. Similar findings were reported for spiral nematode counts. At 33 DA-B, Nimitz at 5 and 7 pt/TA provided a significant reduction in root-knot nematodes compared to the Untreated. By 90 DA-B, all Nimitz rates provided significant nematode control. At 33 DA-B, Nimitz at 5 and 7 pt/TA provided a significant reduction in lesion nematodes compared to the Untreated. By 90 DA-B, all Nimitz rates provided significant nematode control.
2013-2015	Adama Internal Field Trial Sanger, CA	WALNUT Established and badly nematode-damaged	Ring (*Criconemoides sp.*) Stubby Root (*Trichodorus viruliferus*) Lesion (*Scutellonema bradys*)	[3.5, 5.0, 7.0] Micro-sprinkler irrigation	Movento 8 oz/A	**No phyto. reported**; tested as MCW-2; No significant differences in nematode control were observed in this first year of a multi-year study.

			Dagger (*Xiphinema index*)			Higher late season population of Ring species nematodes were higher when MCW2 was applied late in the season compared with the same rate applied earlier in the season, suggesting early timing was more effective. Tree characteristics did not vary significantly after this first season of treatment. Yield was not significantly different across treatments in the first year of this study.

Testimonial Letters Supporting the Use of Nimitz in tree Nuts Production

In testimonial letter 8 from Grow West, Matt Ehlhardt, Director Technical Service, states "Fluensulfone provides growers with an effective too to combat problematic species of Lesion Nematode …offers increased opportunity for integrated approaches…".

Conclusion

Fluensulfone provides pecan and macadamia producers with an effective tool to combat problematic species of root knot nematode (*Meloidogyne* spp.), lesion nematode (*Pratylenchus* spp.), stubby-root nematode (*Trichodorus* spp.) as well as Potato cyst (*Globodera* spp.), Needle (*Longidorus africanus)*, Lance (*Hoplolaimus* spp.), Sting (*Belonolaimus* spp.), and *Paratrichodorus* spp.). Fluensulfone satisfies EPA's criteria:

II: Fluensulfone is an alternative to the minor use pesticide pose greater risks to human health with a softer toxicological profile in comparison to most current pesticides currently registered in the US, decreasing risk of occupational exposure;

III: Fluensulfone will play a significant part in managing pest resistance as a novel MoA against specific nematodes; while keeping a softer effect on other beneficial soil communities;

IV: Fluensulfone will play a significant part of integrated pest management plan as easier to use tool and price competitive in comparison to current fumigant and oxamyl options.

6. Final Conclusions

In conclusion, the data presented in this document demonstrates that Fluensulfone registration on nine or more minor crops meets at least three criteria for granting a three-year extension of the exclusivity data use period under FIFRA Section 3(c) (1) (F) (ii).

Fluensulfone controls selective damaging plant nematodes, while maintain beneficial nematodes on the soil. This compound presents an alternative to current pesticides that pose greater risks to human health and risk of occupational exposure.

Fluelsulfone can be considered a viable and beneficial alternate to fumigants and carbamates that poses greater risks to humans and to the environment.

As a novel mode of action, Fluensulfone plays a significant part in managing pest resistance, and it is easier to use at a completive price in comparison to fumigants and oxamyl options.

The benefits of Fluensulfone were also described in this document by several testimonial letters that received by researchers and extension researchers of NIMITZ.

Therefore, ADAMA US believes that uses and the rationales presented in this document supports the Agency to qualify Fluensulfone for a three-year extension of the exclusivity data use period.

7. References

Adama (Syntech) Internal trial. 2008. “Okra (*Abelmoschus esculentus* Gumbo, variety Clemson Spineless) was planted to test Nimitz 480 SC (MCW-2) in small plots against root knot nematode (*Meloidogyne incognita*)”, Dinuba, CA.

Adama Internal Field Trial. 2009. “Nimitz Nematicide Trial on Cherry”, David Stirling orchard, Kelowna BC.

Adama Internal Field Trial. 2009. “Control of Northern and Columbia Root Knot nematodes in Cantaloupe with MCW”.

Adama Internal Field Trial. 2011-2012. “Efficacy of MCW-2 (Nimitz) for the Control of Soil Disease and Nematodes in Strawberries in Florida; Trial ID: MANA1151”, Dover, FL.

Adama Internal trial. 2014-2015. “Effect of Nimitz Pre-plant Drip Injected in Pepper Nematodes Management”, Immokalee, FL.

Adama Internal Field Trial. 2015. “Evaluation of the Efficacy of Nimitz for the Control of Plant Parasitic Nematodes on Strawberries in Florida; Trial ID: ADA1608F”, Dover, FL – Florida Ag Research Enda Farm.

Adama Internal Field Trial. 2013-2015. “Efficacy of MCW-2 for Nematode Control on Walnuts, Trial ID: MAN1403”, Running Luck Ranch, Pacific Ag Research, Sanger, CA .

Agricular Development Group. 2009. “Control of Northern and Columbia Root Knot nematodes in Cantaloupe with MCW”; Trial # MANA 32253409-6.

Ag Marketing Resource Center 2018.

Becker. 2009. “Control of Northern and Columbia Root Knot nematodes in Cantaloupe with MCW”; Trial # MANA 3254009-4, University of California, Riverside, CA.

Becker, J.O. and Antoon Ploeg. 2015. “Performance of Nimitz in a Carrot Field with High Disease Pressure Caused by the Southern Root-Knot Nematode *Meloidogyne incognita”,* Dept. of Nematology, University of California, Riverside, CA.

Biswas, T., Zhengfei Guan, and Feng Wuhttps://edis.ifas.ufl.edu/fe1028).
Larry Duncan. 2018. “Report of Experimental Results using Nimitz in Laboratory and Field Assays January 14, 2019”, Citrus Research and Educational Center, University of Florida, Lake Alfred, FL.

Brad Booker. 2018. “Nimitz Nematicide Trial on Almond – Microplot”, Pacific Ag, San Luis Obispo, CA.

Booker, Brad. 2018. “Nimitz Nematicide Trial on Citrus – New Establishment.”, Pacific Ag, San Luis Obispo, CA.

Brad Booker. 2018. “Nimitz Nematicide Trial on Peach.”, Pacific Ag, Parlier, CA.

Desaeger, J. 2017 – New Nematode Managemenr Options for Vgetables and Strawberries. Presenttaion GCREC-UF/IFAS (slides)

Dickson, D.W.. 2009. "Efficacy of MCW-2 480 EC for Control of Nematodes in Carrots", Department of Entomology and Nematology, University of Florida, Gainesville, FL.
Duncan, Larry. 2018. "Report of Experimental Results using Nimitz in Laboratory and Field Assays January 14, 2019", Citrus Research and Educational Center, University of Florida, Lake Alfred, FL.

EPA. 2014. Registration Decision for Fluensulfone. A nematicide for use on fruiting vegetables (crop group 8) and cucurbits (crop group 9).

EPA (2015). MEMORANDUM: Fluensulfone - Assessment of the Section 18 Use on Carrots in Michigan. Decision #: 503856. Date: June 19, 2015. 20p.

EPA (2017) PESTICIDE REGISTRATION NOTICE (PRN) 2017-1 - U.S. Environmental Protection Agency. Office of Pesticide Programs. 18 pages.

EPA (2018). MEMORANDUM (PC 103801): Oxamyl: Overview of Usage and Benefits for Banana, Caneberry Carrot, Citrus, Eggplant, Ginger Root, Mint, Peanut, Pineapple, Pome Fruit, Nonbearing Fruit, Sweet Potato and Yams, Tobacco, and Tomato. EPA (Jun 27, 2018). 11p.

EPA (2018) Oxamyl. Proposed Interim Registration Review Decision. Case Number 0253 - June 2018. Docket Number EPA-HQ-OPP- 2010-0028. 38 pages

EPA (2019) MEMORANDUM: Usage and Benefits for Soil Fumigants: Chloropicrin (081501), Dazomet (035602), 1,3-Dichloropropene (029001), Furfural (043301), Metam Sodium (039003), Metam Potassium (039002), and Methyl Bromide (053201). EPA (Sept 24, 2019). 21p.

Holden, David. 2016-2017. "Control Plant Parasitic Nematodes on Strawberry - 2.", Holden Research and Consulting, Ventura, CA.

Jagdale, Ganpati and Timothy Brenneman, and David Shapiro-Ilan. 2018. "Nimitz Nematicide Trial on Pecan.", University of Georgia and USDA-ARS, Dougherty County, GA, and Barwick, GA.

Kawanobe, M.; K. Toyota; T. Fujita and D. Hatta. 2019. Evaluation of Nematicidal Activity of Fluensulfone against Non-Target Free-Living Nematodes under Field Conditions. *Agronomy* (9): 1 – 16p.

Kearn J, Ludlow E, Dillon J, O'Connor V, Holden-Dye L. 2014. Fluensulfone is a nematicide with a mode of action distinct from anticholinesterases and macrocyclic lactones. Pestic Biochem Physiol. 109:44-57.

Miller, Tracy. 2017. "Nimitz Nematicide Trial on Sweet Cherry", Mid Valley Agricultural Services, Linden, CA.

Navia P. 2014a. New nematicide gets to the root of management problems. Agri-view. 5 May 2016. http://www.capitalpress.com/apps/pbcs.dll/article?AID=2014141119957

Navia P. 2014b. New nematicide is a 'step change' away from restricted-use soil fumigants. Southeast Ag Net.
5 May 2016. http://southeastagnet.com/2014/10/29/new-nematicide-is-a-step-change-away-from-restricteduse-soil-fumigants/

Noe, James. 2016. "M. xenoplax pupulations - greenhouse experiments", University of Georgia, Athens, GA.

Noe, James and Ted Holladay. 2018. "Peach Nimitz trials 2018", University of Georgia, Athens, GA.

Noling, J.W. 2015-2016. "Evaluation of NIMITZ in Florida Strawberry.", University of Florida, IFAS, Citrus Research & Education Center, Lake Alfred, FL 33850.

Noling, J.W. 2017. “Evaluation of NIMITZ in Florida Strawberry.”, University of Florida, IFAS, Citrus Research & Education Center, Lake Alfred, FL 33850.

Ojala,John, John Sherod Craig. 2016. “Evaluate Nematicides for Root-Knot Nematode Control in Established Kiwi Vines”, Sun Pacific, Poplar & Earlimart, CA.

Oka Y, Beson M, Barazani A. 2008. MCW-2: a ‘true’ nematicide belonging to the fluoroalkenyl group, in: Proc 5th International Congress of Nematology, Brisbane, Australia, pp. 313–314.

Oka Y, Shuker N, Tkachi N. 2009. Nematicidal efficacy of MCW-2, a new nematicide of the fluoroalkenyl group, against the root-knot nematode Meloidogyne javanica. Pest. Manag. Sci., 65, pp. 1082-1089.

Pacific AG. 2012. “Efficacy of MCW-2 480 EC for Control of Nematodes in Pepper , Trial ID: 3600812-X / R3A1204”, Arroyo Grande, CA.

Phillion D, Ruminski P, Yalamanchili G. 1999. Fluoroalkenyl compounds and their use as pest control agents. US Patent 5 968 916, USA.

Ploeg, et. al. 2015. “Performance of Nimitz in a Sweet Potato Field Infested with *Meloidogyne incognita*.”, Dept. of Nematology, University of California, Riverside, CA.

Ploeg et. al. 2016. “Performance of Nimitz in a Sweet Potato Field Infested with *Meloidogyne incognita*.”, Dept. of Nematology, University of California, Riverside, CA.

Pleog et al. 2019. Control of *Meloidogyne incognita* in sweetpotato with Fluensulfone, J. Nematology 51: 1-8.

Ploeg, A.; Stoddard, S. and Becker, J.O. (2019). Control of *Meloidoyme incognita* is sweetpotato with fluensulfone. *Journal of Nematology* (51): 1-8p.

Shirley, Andrew M. and Andrew P. Nyczepir, Phil M. Brannen1, and James P. Noe. 2018(?). “Use of Fluensulfone in the Post-Plant Management of *Mesocriconema xenoplax* and *Meloidogyne incognita* on Peach”, University of Georgia, Athens, GA and USDA-ARS, SE Fruit & Tree Nut Research Lab, Byron, GA.

Sances, Dr. Frank. 2011. “Control of Root Knot (*Meloidogyne spp.),* Ring CS *(Criconemella spp.),* Stubby Root *(Paratrichodorus minor),* Spiral HD *(Helicotylenchus hihystera),* and Cyst nematode *(Heterodera spp.)* in Strawberry with MCW-2 480 EC”, Pacific Ag Research, San Luis Obispo, CA; Trial # MANA 3498211-1.

USDA, National Ag Statistics Service, 2016.

USDA Economic Research Service 2016.

USDA Economic Research Service 2017.

USDA, National Agricultural Statistics Service, Non-Citrus Fruits and Nuts 2006 Summary, July 2007.

USDA, National Agricultural Statistics Service, Fruit and Nut Report, 2015)

USDA, National Agricultural Statistics Service 2017-2018, Citrus Fruits 2018 Summary, August 2018.

USDA, National Agricultural Statistics Service 2017.

USDA, National Agricultural Statistics Service 2018.

Vallad, G.E.; Siebert, W.J., Adkison,H; Newman , R.S.; Kalb, S., and Hughes, B.S.. 2014. Watermelon (*Citrullus lanatus var. lanatus*) Root-knot nematode; *Meloidogyne incognita* & *M. javanica. Gulf Coast Research and Education*

Center Unversity of Florida, Wumauna, Fl.

Vallad, G.E., H. Adkison, R. Willis, and J. Siebert. 2014. “Effect of isothiocyanate (ITC) fumigants and nematicides on improving plant vigor and reducing root galling of squash and okra in the presence of *Meloidogyne* spp., spring 2014”, Gulf Coast Research and Education Center, University of Florida, GCREC Wimauma, FL.

Westerdahl, B. 2010. “Evaluate Nematicides for Root-Knot Nematode Control and Subsequent Growth of Carrots”, Dept. of Entomology and Nematology, University of California, Davis, CA.

Westerdahl, B. 2015. “Evaluate Nematicides for Root-Knot Nematode Control and Subsequent Growth of Carrots”, Dept. of Entomology and Nematology, University of California, Davis, CA

Westerdahl, Dr. Becky. 2015. “Evaluate Nematicides for Root-Knot Nematode Control and Subsequent Growth of Strawberry”, Dept. of Entomology and Nematology, University of California, Davis, CA.

www.calharvest.com

Appendix 1: Active Ingredient Toxicity Comparison

ACTIVE INGREDIENT TOXICITY COMPARISON

Study	Fluensulfone	Oxamyl	Metham Sodium	Fluopyram	1,3 – D	Chloropicrin
Acute Oral LD_{50}	671 mg/kg	2.5 mg/kg	896 mg/kg	> 2000 mg/kg	224 mg/kg	37.5 mg/kg
EPA Category	Cat III	Cat I	Cat III	Cat III	Cat II	Cat I
Acute Dermal LD_{50}	> 2000 mg/kg	> 2000 mg/kg	> 2000 mg/kg	> 2000 mg/kg	333 mg/kg	-
EPA Category	Cat III	Cat III	Cat III	Cat III	Cat II	-
Acute Inhalation LC_{50}	> 5.1 mg/L	0.056 mg/L	2.54 mg/L	LC_{50} > 5.11 mg/L	3.88 mg/L	0.114 mg/L
EPA Category	Cat IV	Cat II	Cat IV	Cat IV	Cat IV	Cat II
Skin Irritation	Irritating	Non-Irritating	Corrosive	Non-Irritating	Irritating	Irritating
EPA Category	Cat IV	No Classification	Cat I	No Classification	Cat III	Cat II
Eye Irritation	Non-Irritating	Non-Irritating	Non-Irritating	Non-Irritating	Irritating	Irritating
EPA Category	No Classification	No Classification	No Classification	No Classification	Cat II	Cat IV
Skin Sensitization	Sensitizing	Non-Sensitizing	Sensitizing	Non-Sensitizing	Sensitizer	Non-Sensitizing
Genotoxicity	Not Genotoxic	Not Genotoxic	Not Genotoxic	Not Genotoxic	Genotoxic	Not Genotoxic
Carcinogenicity	Non-Carcinogen	Non-Carcinogen	Probable Human Carcinogen	Non-Carcinogen	Probable Human Carcinogen	Non-Carcinogen

Appendix 2: Formulation Acute Toxicity Comparison

Study	Acute Oral LD_{50}	Acute Dermal LD_{50}	Acute Inhalation	Skin Irritation	Eye Irritation	Skin Sensitization
Nimitz 480 EC (Fluensulfone)	> 2000 mg/kg	> 2000 mg/kg	> 6.0 mg/L	Irritating	Irritating	Sensitizing
EPA Category	Cat III	Cat III	Cat IV	Cat IV	Cat III	
Vydate L (Oxamyl)	9 mg/kg	>5000 mg/kg	0.3 mg/L	Non-Irritating	Non-Irritating	Non-Sensitizing
EPA Category	Cat I	Cat IV	Cat II	No Classification	No Classification	
Vydate C-LV (Oxamyl)	9.1 mg/kg	>5000 mg/kg	0.11 mg/L	Non-Irritating	Irritating	Non-sensitizing
EPA Category	Cat I	Cat IV	Cat II	No Classification	Cat II	
Vapam HL (Metham Sodium)	812 mg/kg	> 2000 mg/kg	2.28 mg/L	Irritating	Irritating	Sensitizing
EPA Category	Cat III	Cat III	Cat IV	Cat III	Cat III	
Velum One (Fluopyram)	> 2000 mg/kg	> 2000 mg/kg	> 1.911 mg/L	Non-Irritating	Non-Irritating	Non-Sensitizing
EPA Category	Cat III	Cat III	Cat III	No Classification	No Classification	
Velum Prime (Fluopyram)	> 2000 mg/kg	> 2000 mg/kg	> 1.910 mg/L	Non-Irritating	Non-Irritating	Non-Sensitizing
EPA Category	Cat III	Cat III	Cat III	No Classification	No Classification	
Telone C-17 (1,3-D + Chloropicrin)	304 mg/kg	< 500 mg/kg	105 ppm	Corrosive	Irritant	Sensitizing
EPA Category	Cat III	Cat II	Cat II	Cat I	Cat I	
Telone II (1,3-D + Chloropicrin)	> 110 mg/kg	333 mg/kg	> 2.7 & < 3.07	Irritant	Irritant	Sensitizing
EPA Category	Cat II	Cat II	Cat IV	Cat III	Cat II	

Appendix 3: Formulation Label Requirement Comparison

Study	Toxicological Category	PPE	REI	PHI
Nimitz 480 EC (Fluensulfone) EPA Reg No. 66222-2423	CAUTION	Long-sleeved shirt and long pants; Chemical-resistant gloves; Shoes plus socks; NIOSH-approved respirator with any R or P filter with NIOSH approval number prefix TC-84A.	12 h	Pre-planting
Vydate L (Oxamyl) EPA Reg No. 352-372	DANGER RESTRICTED USE	Coveralls, over long-sleeved shirts and long pants; Chemical resistant gloves; Chemical-resistant foot ware plus socks; Protective eyewear; Chemical-resistant headgear; Chemical resistant apron when cleaning equipment, mixing and loading; NIOSH-approved respirator with any R or P filter with NIOSH approval number prefix TC-84A.	48 h	1-14 Days; Not for Strawberries
Vydate C-LV (Oxamyl) EPA Reg No. 352-532	DANGER RESTRICTED USE	Coveralls, over long-sleeved shirts and long pants; Chemical resistant gloves; Chemical-resistant foot ware plus socks; Protective eyewear; Chemical-resistant headgear for overhead exposure; Chemical resistant apron when cleaning equipment, missing and loading; NIOSH-approved respirator with any R or P filter with NIOSH approval number prefix TC-84A.	48 h	1-14 Days; Not for Strawberries
Vapam HL (Metham Sodium) EPA Reg No. 5481-468	DANGER RESTRICTED USE SPECIFIC-SITE FUMIGANT MANAGEMENT PLAN	All mixers, loaders, other applicators and other handlers must wear; Long-sleeved shirt and long pants; Chemical-resistant gloves, barrier laminate or Viton ≥ 14 mils; Shoes plus socks x A NIOSH-approved respirator with any R or P filter with NIOSH approval number prefix TC-84A .	120 h	Pre-Planting
Velum One & Prime (Fluopyram) EPA Reg No. 264-1078	CAUTION	Long-sleeved shirt and long pants; Chemical-resistant gloves; Shoes plus socks	12 h	Day of harvest
Telone C-17 (1,3-D + Chloropicrin) EPA Reg No. 622719-12	DANGER RESTRICTED USE SPECIFIC-SITE FUMIGANT MANAGEMENT PLAN	All mixers, loaders, other applicators and other handlers must wear; Long-sleeved shirt and long pants; Chemical-resistant gloves, barrier laminate or Viton ≥ 14 mils; Shoes plus socks x A NIOSH-approved respirator with any R or P filter with NIOSH approval number prefix TC-84A.	-	-
Telone II (1,3-D) EPA Reg No. 622719-32	WARNING RESTRICTED USE SPECIFIC-SITE FUMIGANT MANAGEMENT PLAN	All mixers, loaders, other applicators and other handlers must wear; Long-sleeved shirt and long pants; Chemical-resistant gloves, barrier laminate or Viton ≥ 14 mils; Shoes plus socks x A NIOSH-approved respirator with any R or P filter with NIOSH approval number prefix TC-84A.	-	-

Appendix 4: Section 18 for the Michigan Department of Agriculture (2015) – Carrots

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

OFFICE OF
CHEMICAL SAFETY
AND POLUTION PREVENSION

MEMORANDUM

Date: 19 June 2015

Subject: Fluensulfone – Assessment of the Section 18 Use on Carrots in Michigan

PC Code: 050410	DP Barcode: D427229
Decision No.: 503856	Registration No.: 66222-243
Petition No.: 15MI05	Regulatory Action: Section 18
Risk Assessment Type: Single Chemical Aggregate	Case No.: None
TXR No.: NA	CAS No.: 318290-98-1
MRID No.: None	40 CFR: 180.680

From: Michael A. Doherty, Ph.D., Senior Chemist
Zaida Figueroa, M.S., Industrial Hygienist
Health Effects Division (HED; 7509P)
Risk Assessment Branch II (RAB II)

Through: Christina Swartz, Chief
HED, RAB II

To: Stacey Groce/Tawanda Maignan (Team 09)
Marion Johnson, Chief
Registration Division (RD; 7505P)
Risk Integration, Minor Use, and Emergency Response Branch

Introduction

The Michigan Department of Agriculture has issued a crisis exemption for the use of fluensulfone to control a number of nematode species in carrot fields. This is the first Section 18 exemption for this use. Under the exemption, up to 2,000 acres of carrot fields will be treated with the Nimitz® 480 EC formulation of fluensulfone (EPA Registration No. 66222-243). The Section 18 documentation indicates that the use will be in counties of Lapeer, Montcalm, Newaygo, and Oceana. The use season is 14 April to 15 June 2015, and the crisis exemption was issued on 14 April 2015.

Fluensulfone {5-Chloro-2-[(3,4,4-trifluoro-3-buten-1-yl)sulfonyl]thiazole} is a nematicide registered in 2014 for use on cucurbit and fruiting vegetables, and the Agency has received a Section 3 request to register this ingredient for use on additional crops, including carrot.

Agency Memoranda Used to Support this Section 18 Exemption Risk Assessment

D403767. M. Doherty, J. D'Agostino, Z. Figueroa. 18 June 2014. Fluensulfone – New Active Ingredient Human Health Risk Assessment of Proposed Uses on Cucurbit Vegetables and Fruiting Vegetables.

D403813. M. Doherty. 4 June 2014. Fluensulfone. Petition for the Establishment of Permanent Tolerances and Registration for Use of the New Active Ingredient on Fruiting Vegetables (Crop Group 8-10) and Cucurbit Vegetables (Crop Group 9). Summary of Analytical Chemistry and Residue Data from the OECD Joint Review.

D403814, Z. Figueroa, 18 July 2014. Fluensulfone. Occupational and Residential Exposure and Risk Assessment to Support the Registration of the New Active Ingredient on Cucurbits and Fruiting Vegetables.

D418204, M. Doherty, 10 June 2014. Fluensulfone Acute and Chronic Aggregate Dietary (Food and Drinking Water) Exposure and Risk Assessments for the First Food Use Section 3 Registration Action on Fruiting and Cucurbit Vegetables

Assessment Summary

Chemical Identity and Background Information. Fluensulfone {5-Chloro-2-[(3,4,4-trifluoro-3-buten-1-yl)sulfonyl]thiazole} is the first nematicide in the fluoroalkenyl class and was registered as a new active ingredient in the U.S. in September of 2014. It is registered for pre-plant application by broadcast spray or drip irrigation seven days prior to transplanting cucurbit and fruiting vegetables. Tolerances for residues in those crop groups are established at 0.50 ppm, with enforcement based solely on residues of the trifluorobutene sulfonic acid metabolite (expressed in terms of fluensulfone; 40 CFR 180.680). Risk assessments for fluensulfone are based on residues of the parent compound, *per se*, due to the low toxicity of the butene sulfonic acid and thiazole sulfonic acid metabolites. There are no Canadian or Codex MRLs for residues of fluensulfone in carrot at this time, and international harmonization is not an issue for this Section 18.

Section 18 Use Pattern Information. Under the specific exemption, fluensulfone is applied as a single, pre-plant application to carrot fields by broadcast spray, banded spray, or drip irrigation. Application will precede planting by no less than 14 days, and the applied material will be watered into the soil two to five days after application. The maximum application rate is 2.5 lb a.i./A, with the rate prorated to the actual treated area in the case of banded spray application.

Toxicological Information. The toxicology database for fluensulfone is complete for purposes of conducting an FQPA human health risk assessment. In mammals, exposure to fluensulfone results in effects on the hematopoietic system (decreased platelets, increased white blood cells, hematocrit, and reticulocytes), kidneys, and lungs. Changes in clinical chemistry as well as in body weight were also observed across multiple studies and species. In rats, pup loss was noted, with the majority of deaths occurring on post-natal day 2. Overall, the most sensitive endpoints for assessing human health risk are the increased pup-loss effects for acute dietary exposure; body weight, hematological and clinical chemistry changes for chronic dietary and dermal exposures (short/intermediate term); and clotting time, decreased thymus weight, and portal-of-entry effects (histopathology of the epiglottis and nasal cavity) for inhalation exposures (short/intermediate term). Given the overall completeness of the toxicity database, the lack of uncertainty regarding susceptibility of infants and children, and the conservatisms in the human health exposure estimates, HED has reduced the Food Quality Protection Act Safety Factor (FQPA SF) from 10X to 1X. For assessing occupational oral and dermal exposures, the standard inter- and intra-species uncertainty factors of 10X are appropriate and result in a level of concern (LOC) of 100. For assessing occupational inhalation exposure, the interspecies (to account for differences between rats and humans) factor has been reduced to 3X; however, an additional 10X factor is required because a no-observed-adverse-affect level (NOAEL) was not found for the portal-of-entry effects, resulting in an LOC of 300.

Table 1. Summary of Toxicological Doses and Endpoints for use in Fluensulfone Dietary and Non-Occupational Human Health Risk Assessments.

Exposure/ Scenario	Point of Departure	Uncertainty/ FQPA Safety Factors	RfD, PAD, Level of Concern for Risk Assessment	Study and Toxicological Effects
Acute Dietary (All Populations, including Infants and Children and Females 13-49 years of age)	Offspring NOAEL= 16.2/23.0 mg/kg/day (M/F)	UF_A= 10x UF_H=10x FQPA SF= 1x	Acute RfD = 0.16 mg/kg/day aPAD = 0.16 mg/kg/day	2-generation reproduction – rat Offspring LOAEL = 122.0/169.1 mg/kg/day (M/F) based on an increase in pup loss between PND 1 and 4 in the F1 and F2 offspring with the majority of deaths occurring on day 2.

Table 1. Summary of Toxicological Doses and Endpoints for use in Fluensulfone Dietary and Non-Occupational Human Health Risk Assessments.

Exposure/ Scenario	Point of Departure	Uncertainty/ FQPA Safety Factors	RfD, PAD, Level of Concern for Risk Assessment	Study and Toxicological Effects
Chronic Dietary (All Populations)	NOAEL = 3.1 mg/kg/day	UF_A= 10x UF_H=10x FQPA SF= 1x	Chronic RfD = 0.03 mg/kg/day cPAD = 0.03 mg/kg/day	Co-critical 90-day dog and chronic dog Chronic: LOAEL = 16 mg/kg/day based on decreased body weight, increased mean hemoglobin concentration distribution width, and increased relative and absolute reticulocyte counts in both sexes, decreased prothrombin time in males and increased platelets in females. Subchronic: NOAEL = 1.6 mg/kg/day LOAEL = 17.1 mg/kg/day based on decreased body weight in females and increased relative and absolute reticulocyte counts, decreased bilirubin, decreased albumin, decreased A/G ratio, increased TSH, and pigmented Kupffer cells in both sexes.
Incidental Oral All Durations	A dose and endpoint for incidental oral exposure were not selected because there are presently no residential uses for fluensulfone.			
Dermal All Durations	There are presently no residential uses for fluensulfone.			
Inhalation All Durations	There are presently no residential uses for fluensulfone.			
Cancer (oral, dermal, inhal.)	Classification: Suggestive evidence of carcinogenicity in humans based on lung tumors in female rats. The RfD is protective of potential cancer effects.			

Point of Departure (POD) = A data point or an estimated point that is derived from observed dose-response data and used to mark the beginning of extrapolation to determine risk associated with lower environmentally relevant human exposures. NOAEL = no observed adverse effect level. LOAEL = lowest observed adverse effect level. UF = uncertainty factor. UF_A = extrapolation from animal to human (interspecies). UF_H = potential variation in sensitivity among members of the human population (intraspecies). UF_L = use of a LOAEL to extrapolate a NOAEL. FQPA SF = FQPA Safety Factor. PAD = population adjusted dose (a = acute, c = chronic). RfD = reference dose.

Table 2. Summary of Toxicological Doses and Endpoints for use in Fluensulfone Occupational Human Health Risk Assessments.

Exposure/ Scenario	Point of Departure	Uncertainty Factors	Level of Concern for MOE	Study and Toxicological Effects
Dermal Short- and Intermediate-Term (1-30 days and 1-6 months)	NOAEL= 3.1 mg/kg/day DAF = 40.9%	UF_A=10x UF_H=10x	Occupational LOC for MOE = 100	Co-critical 90-day dog and chronic dog Chronic: LOAEL = 16 mg/kg/day based on decreased body weight, increased mean hemoglobin concentration distribution width, and increased relative and absolute reticulocyte counts in both sexes, decreased prothrombin time in males and increased platelets in females. Subchronic: NOAEL = 1.6 mg/kg/day LOAEL = 17.1 mg/kg/day based on decreased body weight in females and increased relative and absolute reticulocyte counts, decreased bilirubin, decreased albumin, decreased A/G ratio, increased TSH, and pigmented Kupffer cells in both sexes.
Inhalation Short- and Intermediate-Term (1-30 days and 1-6 months)	NOAEL= not established (<0.04 mg/L) [a]HEC = 0.00429 mg/L [b]HED = 0.244 mg/kg/day (low breathing rate), = 0.491 mg/kg.day (medium breathing rate), = 0.853 mg/kg/day (high breathing rate)	UF_A=3x UF_H=10x UF_L=10x	Occupational LOC for MOE = 300	90-day inhalation toxicity – rat LOAEL = 0.04 mg/L (lowest dose tested) based on weight loss in males, prolonged prothrombin time in females, decreased thymus weight in males, histopathological changes in the epiglottis in both sexes, and histopathological changes in the nasal cavity of males.
Cancer (oral, dermal, inhal.)	Classification: Suggestive evidence of carcinogenicity in humans based on lung tumors in female mice. The RfD is protective of potential cancer effects.			

Point of Departure (POD) = A data point or an estimated point that is derived from observed dose-response data and used to mark the beginning of extrapolation to determine risk associated with lower environmentally relevant human exposures. NOAEL = no observed adverse effect level. LOAEL = lowest observed adverse effect level. UF = uncertainty factor. UF_A = extrapolation from animal to human (interspecies). UF_H = potential variation in sensitivity among members of the human population (intraspecies). UF_L = use of a LOAEL to extrapolate a NOAEL. MOE = margin of exposure. LOC = level of concern. DAF = dermal absorption factor

[a] HEC = rat NOAEL x (daily duration adjustment) x weekly daily duration adjustment x RDDR =0.04 mg/L x (6 hr/8 hr) x (1) x 0.143 = 0.00429 mg/L.

[b] HED = HEC x human specific conversion factor x activity factor for the exposure scenario x daily duration = 0.00429 mg/L x 11.8 L/hr-kg x (0.6, 1.2, and 2.1 for low, medium, and high, respectively) x 8 hr.

Occupational Exposure and Risk Information. Occupational exposures and risks from the use of fluensulfone on cucurbit and fruiting vegetables were estimated in the last risk assessment, with margins of exposure (MOEs) ranging from 81 to 270 for dermal exposure (level of concern is dermal MOE < 100) and from 290 to 1,300 for inhalation exposure (level of concern is inhalation MOE < 300). Exposure inputs are the same for carrot as those used in the previous assessment for cucurbit and fruiting vegetables. Therefore, HED is translating the previous occupational handler assessment to this Section 18 assessment.

HED notes that in the previous occupational assessment, use of personal protective equipment (PPE) in the form of chemical-resistant gloves and engineering controls was necessary to achieve dermal MOEs above the LOC. The Section 18 label for use on carrot should specify the same PPE as is listed on the Section 3 label for cucurbit and fruiting vegetables.

Due to the use pattern and application timing (i.e., applied as a pre-plant broadcast application prior to transplanting), no post-application exposure is expected for workers re-entering treated areas. Fluensulfone is classified as Toxicity Category III via the dermal route and Toxicity Category IV for skin and eye irritation potential. It is a skin sensitizer. The REI of 12 hours listed on the label is adequate to protect agricultural workers from post-application exposures to fluensulfone.

Dietary Exposure Information. The registrant has petitioned the Agency to register fluensulfone for use on a number of additional crops, including carrots. In order to support that registration request, the registrant provided data from supervised residue trials in carrot. Those data show quantifiable residues of fluensulfone as well as the sulfonic acid metabolites in carrots harvested from fluensulfone-treated fields. In estimating dietary risk, HED used the maximum average field trial fluensulfone residue value from the carrot study, the residue levels used in the previous dietary assessment for fluensulfone (0.01 ppm for cucurbit and fruiting vegetables), and an assumption of 100% crop treated for all commodities. Modeled estimates of residues in drinking water are the same as those used in the previous Section 3 risk assessment and are considered to be conservative, and therefore protective of potential residues in drinking water resulting from the Section 18 use on carrots. The resulting screening-level dietary risk estimates across all representative population groups range from 2% to 8% of the PAD for acute exposure and from 3% to 11% of the PAD for chronic exposure, and all dietary risk estimates are not of concern.

Residential Exposure Information. At this time, there are no uses for fluensulfone that would result in direct non-dietary exposure in a residential or recreational setting.

Aggregate Risk Information. Aggregate risk estimates are equivalent to the dietary risk estimates and are not of concern for all population groups/scenarios.

Cumulative Risk Information. The Agency has not made a determination that fluensulfone shares a common mechanism of toxicity with other compounds and has not conducted a cumulative risk assessment which includes fluensulfone.

Conclusions. HED has no objection to the issuance of this Section 18 exemption. The available data support a tolerance for residues of fluensulfone in/on carrot (as measured by residues of the BSA metabolite expressed in parent-equivalents) at 2.0 ppm. RD should ensure that the Section 18 label for use on carrot has the same PPE as is currently listed on the Section 3 label for use on cucurbit and fruiting vegetables.

Toxicological Considerations

For complete details, see D403767, M. Doherty *et al*., 18 June 2014.

The hematopoietic system was the major target of fluensulfone activity in rats, dogs, and mice. Effects on the hematopoietic system included increased white blood cells (rats and mice), increased hematocrit (mice), decreased platelets (mice), and increased reticulocytes (dogs) in subchronic dietary studies at the lowest observable effect levels (LOAEL) with additional effects on the hematopoietic system observed at higher doses. Effects on the hematopoietic system were also observed in chronic dietary studies for all species and, in the case of the chronic rat and dog studies, these effects were observed at the LOAELs. Effects on the hematopoietic system are consistent with results from rat metabolism studies which demonstrated that fluensulfone can react with the free thiol moiety of globin, forming a covalent linkage to the thiazole group displacing butene sulfinic acid. This led to slower elimination of the thiazole portion of fluensulfone from whole blood (time from dose to 50% of peak concentration, DT_{50} = 6-9 days) compared to plasma (DT_{50} = 16-17 hours).

Other effects commonly observed in the toxicological database in all three species included changes in clinical chemistry parameters and decreased body weights, both of which were often seen at the LOAELs in subchronic and chronic studies. Altered clinical chemistry parameters included decreased plasma alanine amino transferase (ALAT, rats and dogs), increased cholesterol (rats), increased triglycerides (rats), increased phospholipids (rats), increased bilirubin (mice) or decreased bilirubin (dogs), decreased protein (dogs), decreased albumin and albumin/globulin ratio (dogs), decreased glucose (dogs), and increased TSH (dogs) in subchronic studies. For the hematological, clinical chemistry, and body weight effects observed in all three species, the dog appeared to be slightly more sensitive than mice and rats.

Fluensulfone also caused effects on the kidney in male rats; however, the effects are consistent with accumulation of α-2-microglobulin which has been deemed not relevant to humans (USEPA 1991).

Effects on the lung were observed following chronic dietary exposure in mice and rats. These effects consisted of an increased incidence and severity of lung interstitial inflammation in the 2-

year rat study and an increased incidence of bronchiolization (change from flattened epithelium to cuboidal epithelium) in the 18-month mouse study.

Fluensulfone also appeared to cause portal-of-entry effects in rats. This included the forestomach (diffuse basal cell hyperplasia) and pharynx (mononuclear infiltrates) in dietary subchronic studies; the epiglottis (squamous metaplasia, epithelial hyperplasia, and focal mononuclear cell infiltrates) and nasal cavity (squamous epithelial hyperplasia) in the 90-day inhalation study; and an increased incidence/severity of acanthosis/hyperkeratosis in the 28-day dermal study. The dermal effects were considered adaptive due to the moderate degree of acanthosis/hyperkeratosis observed.

Discoloration of teeth was noted in two subchronic toxicity studies, and increased levels of total fluoride were observed with a strong dose-response across numerous studies. Neither the discoloration nor the increased flouride levels are considered adverse (i.e., severe dental fluorosis); however, they do indicate that exposure to fluensulfone may contribute to overall fluoride exposure. Residue data (see previous risk assessment) demonstrate that total fluoride levels are indistinguishable between fluensulfone-treated and untreated crops; therefore, HED has concluded that for the assessed uses, fluensulfone is not a source of fluoride exposure.

There was no evidence of immunotoxicity in the available studies, which included a guideline immunotoxicity study in the rat. There is limited evidence that fluensulfone results in effects on the nervous system. Decreased locomotor activity, decreased spontaneous activity, decreased rearing, and impaired righting response was observed only on Day 1 following acute exposure in the acute neurotoxicity study. In contrast, no evidence suggestive of neurotoxicity was observed in any other study, including a subchronic neurotoxicity study. Following dermal exposure for 28-days, systemic effects including increased reticulocytes and increased cholesterol were observed, but only at a dose twice that of the limit dose.

There was evidence of increased qualitative susceptibility of pups to the effects of fluensulfone. Decreased pup weight, decreased spleen weight, and an increase in post-natal pup loss [post-natal days (PND) 1-4] were observed in the rat two-generation reproductive toxicity study at a dose causing decreased body weight in the parents. The findings in the pups were considered more severe than those seen in the maternal animals. No evidence of increased quantitative or qualitative susceptibility was seen in developmental toxicity studies in rats and rabbits. In the rat developmental toxicity study, decreased fetal weight was observed in the presence of decreased body weight in maternal animals. In the rabbit developmental toxicity study, decreased fetal weight and incomplete ossification of digit 5 of the medial phalanx in both forelimbs were observed in the presence of decreased body weight in maternal animals.

Chronic dietary exposure to fluensulfone in female mice resulted in an increased incidence of lung adenomas and carcinomas. The Cancer Assessment Review Committee (CARC) classified fluensulfone as having "Suggestive Evidence of Carcinogenicity" based on an increased incidence of alveolar/bronchiolar adenomas and carcinomas in the lung of mid- and high-dose female mice in the oncogenicity study. All genotoxicity studies that were conducted on fluensulfone and three of its metabolites (thiazole sulfonic acid; TSA, butene sulfonic acid; BSA, and methyl sulfone; MeS) were negative, except for MeS with *Salmonella typhimurium* strain TA 100 in the absence of metabolic activation during a bacterial reverse mutation assay.

Testing in acute lethality studies with fluensulfone technical-grade material resulted in low toxicity classifications via the oral (Toxicity Category III), dermal (Toxicity Category III), and inhalation (Toxicity Category IV) routes of exposure. Fluensulfone technical-grade material was not an irritant to eyes (Toxicity Category IV) or skin (Toxicity Category IV) but was a skin sensitizer. Similar results were obtained in acute lethality studies with an emulsifiable concentrate formulation (480 EC).

Oral acute lethality studies were also conducted with the metabolites MeS, BSA, or TSA, each at 2000 mg/kg bw. By the oral route of exposure, MeS was of moderate toxicity (Toxicity Category II) and both BSA and TSA were of low toxicity (Toxicity Category III). HED notes that all animals treated with BSA or TSA survived the entire study period and that the toxicity category for those metabolites is based on the dosing level rather than on actual LD_{50} estimates. Furthermore in the BSA and TSA acute toxicity studies, body weights of all animals were within the normal range, no macroscopic findings were recorded at necropsy, and no clinical signs were observed except in three animals which exhibited slightly ruffled fur two hours after administration of TSA, which persisted up to the three-hour observation in two animals. In 28-day oral toxicity studies with BSA and TSA, no treatment-related effects were observed at any dose (limit-dose = 1000 mg/kg/day).

Safety Factor for Infants and Children (FQPA Safety Factor)

The toxicology and the exposure databases for fluensulfone support a reduction of the required 10X FQPA SF to 1X based on the following considerations: the completeness of the toxicity database including adequate studies to assess the potential susceptibility in the young; there is no indication of quantitative susceptibility in the developmental and reproductive toxicity studies, and there are no residual uncertainties concerning pre- or post-natal toxicity; the endpoints and doses chosen for risk assessment are protective of the qualitative susceptibility observed in the 2-generation reproduction study; acute and subchronic neurotoxicity studies (ACN and SCN) are available. In addition, all endpoints used in the risk assessment are protective of the evidence of neurotoxicity observed in the ACN, and a developmental neurotoxicity study is not required. The dietary assessment is based on reliable data and conservatively modeled drinking water residues, and will not underestimate exposure. Finally, there are no registered or requested uses for fluensulfone that would result in residential exposure.

Occupational Exposure Considerations

There is a potential for occupational exposure associated with handler activities (i.e., mixing, loading, and applying). Given that the Section 18 use pattern requires soil-incorporated application 14 days before planting, no post-application exposure is expected for workers re-entering treated areas. The duration of exposure for the uses on cucurbit and fruiting vegetables is expected to be short-term (1-30 days) and intermediate-term (1-6 months). For the Section 18 use, similar durations of exposure may occur. Long-term exposures (greater than 6 months) are not anticipated.

The occupational handler (mixer, loader, applicator) exposure and risk estimates from the previous assessment are summarized in Table 3. Note that in order to mitigate occupational risk issues, the originally proposed application rate of 3.5 lb a.i./A was reduced to 2.5 lb a.i./A on the registered Section 3 label, which matches the application rate on the Section 18 label.

Table 3. Short- and Intermediate-Term Occupational Handler Non-Cancer Exposure and Risk Estimates for Fluensulfone. Taken from D403814, Z. Figueroa, 18 July 2014.

Exposure Scenario	Mitigation Level[a]	Application Rate[b]	Area Treated[c]	Dermal Dose[d] (mg/kg/day)	Dermal MOE[e]	Inhalation Dose[f] (mg/kg/day)	Inhalation MOE[g]
Mixing/Loading Liquids for Chemigation (AHETF/PHED)	Baseline	1.75 lb ai/A	350 A	0.69	5	0.00168	290
	Engineering Controls			0.0269	120	0.000635	770
	Baseline	2.50 lb ai/A		0.9870	3.1	0.002400	200
	Engineering Controls			0.0385	81	0.000908	540
Mixing/Loading Liquids for Groundboom (AHETF/PHED)	Baseline	1.75 lb ai/A	80 A	0.157	20	0.000384	1,300
	Single Layer, Gloves, No Respirator			0.0269	120	0.000384	1,300
	Baseline	2.50 lb ai/A		0.2250	14	0.000548	900
	Single Layer, Gloves, No Respirator			0.0384	81	0.000548	900
Applying Liquids for Groundboom Application (AHETF/PHED)	Baseline	1.75 lb ai/A	80 A	0.0562	60	0.000595	410
	Single Layer, Gloves, No Respirator			0.0115	270	0.000595	410
	Baseline	2.50 lb ai/A		0.0803	40	0.00085	290
	Single Layer, Gloves, No Respirator			0.0165	190	0.00085	290

a. Mitigation level or PPE. Baseline = long-sleeved shirt, long pants, shoes, socks, no gloves, no respirator.

b. Application Rates based on proposed use on label (3.5 lb ai/A for all crops).

c. Exposure Science Advisory Council Policy No. 9.1.

d. Dermal Dose (mg/kg/day) = Daily Unit Exposure (μg/lb ai) x Dermal Absorption Factor (40.9%) x Application Rate (lb ai/gal) x Area Treated / Body Weight (80 kg).

e. Dermal MOE = NOAEL (3.1 mg/kg/day) / Dermal Daily Dose (mg/kg/day). LOC = 100.

f. Inhalation Dose (mg/kg/day) = Daily Unit Exposure (μg/lb ai) x Application Rate (lb ai/acre) x Acres Treated / Body Weight (80 kg).

g. Inhalation MOE = HED (0.491 $mg/kg/day_{M/L}$ or 0.244 $mg/kg/day_{A}$) / Inhalation Daily Dose (mg/kg/day). LOC = 300.

Residue Chemistry Considerations

For details regarding the core residue chemistry studies, see D403813 (M. Doherty, 4 June 2014).

Metabolic Fate. Studies depicting the nature of the residues in target crops (tomato, potato, and lettuce), rotational crops (radish, lettuce, and wheat) and livestock (laying hens and lactating goats) consistently show fluensulfone to be cleaved at the sulfonyl moiety, presumably via glutathione conjugation, resulting in both halves of the molecule having a sulfonyl functional group. Parent fluensulfone was identified only in poultry fat and in rotational lettuce, radish foliage, and wheat hay, forage and straw at short plant-back intervals (30 days). With the exception of poultry fat, fluensulfone was not a major residue in any matrix. In both target and rotational crops, the cleavage products form thiazole sulfonic acid (TSA) and butene sulfonic acid (BSA). The butene sulfonic acid may then be oxidized to form smaller compounds that are incorporated into natural plant components or mineralized to CO_2. In livestock, the majority of the radiolabel was excreted. Retained fluensulfone is extensively metabolized, with the radioactivity being associated primarily with amino acids and triglycerides. Thiazole methyl sulfone and butene sulfinic acid were identified in livestock studies, but were observed only in excreta. In the rat metabolism study, significant residues were thiazole mercapturate, thiazole glucuronide, thiazole sulfonic acid, butene sulfinic acid, and butene sulfonic acid. These are all consistent with the glutathione-conjugation process noted in the other metabolism studies. Fluensulfone was not detected as a significant residue (i.e., < 0.1% of the applied dose) in rats.

Toxicology data for the TSA and BSA metabolites show that they are non-toxic at levels expected in foods. As a result, inclusion of the parent compound in risk assessment, even at the limit of quantitation, is considered adequate to address risks that may be present from dietary exposure to TSA and BSA.

Enforcement of tolerances should be via measurement of residues of BSA only. The parent compound alone is a poor indicator of misuse due to the lack of consistently quantifiable residues. The metabolites TSA and BSA both appear at quantifiable levels in the crop field trials and are good candidates for marker compounds. The TSA metabolite may persist from one year to the next; therefore, the potential for TSA to accumulate makes BSA a better indicator of misuse.

Table 4. Summary of Metabolites and Degradates to be included in the Risk Assessment and Tolerance Expression of Fluensulfone.

Matrix		Residues Included in Risk Assessment	Residues Included in Tolerance Expression
Plants	Primary Crop	Fluensulfone	BSA*, as parent equivalent
	Rotational Crop	Fluensulfone	BSA*, as parent equivalent
Livestock	Ruminant	None	None
	Poultry	None	None

Table 4. Summary of Metabolites and Degradates to be included in the Risk Assessment and Tolerance Expression of Fluensulfone.		
Matrix	Residues Included in Risk Assessment	Residues Included in Tolerance Expression
Drinking Water	Fluensulfone + MeS* + deschloro-fluensulfone, expressed as parent equivalent	Not Applicable

* BSA refers to the butene sulfonic acid metabolite (3,4,4-trifluoro-but-3-ene-1-sulfonic acid; Company Code M-3627); MeS refers to the methyl sulfone metabolite (5-chloro-2-methyl sulfonyl thiazole; Company Code M-3626).

Analytical Methods. An analytical method suitable for enforcement purposes has been approved by the Agency (D403813, M. Doherty, 4 June 2014). That same method was used in the field trials for carrot and was shown to be appropriate for that crop. The method has an LOQ, defined as the lower limit of method validation, of 0.01 ppm. For carrot, the method has a calculated LOQ of 0.005 ppm.

Residue Chemistry. The registrant submitted a study volume (MRID 49553613) depicting crop field trials conducted in carrot. The study was submitted in support of several newly petitioned-for uses. In that study, 1 field trial was conducted each in Florida, Texas, New Mexico, Ohio, Washington, Nova Scotia, and Quebec; two trials were conducted in Ontario, and three trials were conducted in California (12 trials total). A granular formulation of fluensulfone was applied at 3.6 lb a.i./A (nominal), 6-8 days prior to planting. The applied material was incorporated into the soil by tilling. Carrots were harvested at maturity and sent to Golden Pacific Laboratories for analysis. Samples were stored frozen for up to 526 days; and residues were shown to be stable based on concurrent storage stability data. Residues in/on carrot ranged from <0.01 to 0.495 ppm for fluensulfone and from <0.01 to 1.24 ppm for BSA.

The results from the field trials may overestimate residues in/on carrot treated as part of the Section 18 exemption due to the exaggerated rate (3.6 vs. 2.5 lb a.i./A), use of a granular rather than a liquid product, and the shorter pre-plant interval (7 vs. 14 days). Using the results from the field trials as input to the OECD MRL/tolerance calculation procedures results in a tolerance for residues of fluensulfone (based on BSA as parent-equivalent) of 2.0 ppm.

Processed Food and Feed. There are no significant processed food/feed items associated with carrot.

Meat, Milk, Poultry, and Eggs. Carrot culls may be fed to dairy cattle. At this time, there are no other livestock feedstuffs associated with registered uses of fluensulfone. Studies delineating the metabolism of fluensulfone in livestock commodities indicates that the parent compound is cleaved forming BSA as an intermediate compound. Metabolism continues such that fluensulfone, and by extension BSA, is further broken down into its constituent components and incorporated into natural products. Based on OPP's understanding of the metabolism of fluensulfone in livestock animals and on the low proportion of carrot culls as a livestock feed item (maximum of 10% in a reasonably balanced modeled diet), there is no expectation of finite residues of BSA in livestock commodities, including milk; therefore, tolerances for residues of fluensulfone in livestock commodities are not needed at this time [40 CFR 180.6(a)(3)].

Rotational Crop Restrictions. The Section 18 label specifies that only crops on the registered label may be planted into a field within 1 year of applying the product.

International Residue Limits. At this time, there are no CODEX or Canadian MRLs that will impact the setting of tolerances for this Section 18 exemption.

Dietary Exposure Analysis

Acute and chronic aggregate dietary (food and drinking water) exposure and risk assessments were conducted using the Dietary Exposure Evaluation Model software with the Food Commodity Intake Database (DEEM-FCID) Version 3.16, which uses 2003-2008 food consumption data from the U.S. Department of Agriculture's National Health and Nutrition Examination Survey, What We Eat in America, (NHANES/WWEIA).

As previously noted, the residue of concern for dietary risk assessment is the parent compound fluensulfone. The maximum fluensulfone residue observed in the carrot field trials was 0.495 ppm. HED has updated the previous dietary exposure and risk assessment (D418204, M. Doherty, 10 June 2014) to reflect a 0.5-ppm residue level on all carrot (i.e., 100% crop treated).

As an estimated drinking water concentration of fluensulfone, HED used the values previously provided by EFED: 77.6 ppb for acute and 52.5 ppb for chronic (D417634, J. Lin, January 2014).

The dietary exposure and risk estimates should be considered screening-level estimates that likely overestimate actual exposures to fluensulfone that may result from the Section 18 use on carrot. Generally, HED is concerned when dietary risk estimates exceed 100% of the population-adjusted dose for any of the representative populations within the consumption database (general U.S. population, infants, children 1-2 years old, children 3-5 years old, children 6-12 years old, youth 13-19 years old, adults 20-49 years old, adults 50-99 years old, and females 13-49 years old). For fluensulfone, the dietary risk estimates are not of concern for all population groups and for both acute and chronic exposure scenarios (Table 5). Complete input and output listings for the dietary exposure analysis are provided in Attachments 2-5.

Table 5. Summary of Acute and Chronic Dietary Exposure and Risk Estimates for Fluensulfone.

	Acute (95th Percentile)		Chronic	
Population Subgroup	Exposure, mg/kg/day	Risk, % aPAD	Exposure, mg/kg/day	Risk, % cPAD
Total US Population	0.0045	2	0.0012	4
All Infants	0.0138	8	0.0034	11
Children 1-2	0.0072	4	0.0019	6
Children 3-5	0.0058	3	0.0015	5
Children 6-12	0.0042	2	0.0011	4
Youth 13-19	0.0036	2	0.0009	3
Adults 20-49	0.0043	2	0.0012	4

Table 5. Summary of Acute and Chronic Dietary Exposure and Risk Estimates for Fluensulfone.				
	Acute (95th Percentile)		Chronic	
Population Subgroup	Exposure, mg/kg/day	Risk, % aPAD	Exposure, mg/kg/day	Risk, % cPAD
Adults 50-99	0.0039	2	0.0012	4
Female 13-49	0.0043	2	0.0012	4

Residential Exposure

At this time, there are no registered uses of fluensulfone that will result in direct residential exposure.

Spray Drift

Spray drift is a potential source of exposure to those nearby pesticide applications. This is particularly the case with aerial application, but, to a lesser extent, spray drift can also be a potential source of exposure from the ground application methods (e.g., groundboom) employed for fluensulfone. The Agency has been working with the Spray Drift Task Force (a task force composed of various registrants which was developed as a result of a Data Call-In issued by EPA), EPA Regional Offices and State Lead Agencies for pesticide regulation and other parties to develop the best spray drift management practices (see the Agency's Spray Drift website for more information)[1]. The Agency has also developed a policy on how to appropriately consider spray drift as a potential source of exposure in risk assessments for pesticides.

The potential for spray drift will be quantitatively evaluated for each pesticide during the Registration Review process which ensures that all uses for that pesticide will be considered concurrently. The approach is outlined in the revised (2012) Standard Operating Procedures for Residential Risk Assessment (SOPs) - Residential Exposure Assessment Standard Operating Procedures Addenda 1: Consideration of Spray Drift. This document outlines the quantification of indirect non-occupational exposure to drift.

Residential Bystander Post-Application Inhalation Exposure

Volatilization of pesticides may be a source of post-application inhalation exposure to individuals nearby pesticide applications. The Agency sought expert advice and input on issues related to volatilization of pesticides from its Federal Insecticide, Fungicide, and Rodenticide Act Scientific Advisory Panel (SAP) in December 2009, and received the SAP's final report on March 2, 2010 (http://www.epa.gov/scipoly/SAP/meetings/2009/120109meeting.html). The Agency has evaluated the SAP report and has developed a Volatilization Screening Tool and a subsequent Volatilization Screening Analysis (http://www.regulations.gov/#!docketDetail;D=EPA-HQ-OPP-2014-0219). During Registration Review, the Agency will use this analysis to determine if data (i.e., flux studies, route-specific inhalation toxicological studies) or further analysis is required for fluensulfone.

[1] Available: http://www.epa.gov/opp00001/factsheets/spraydrift.htm.

Aggregate Risk

In accordance with the FQPA, HED must consider and aggregate (add) pesticide exposures and risks from three major sources: food, drinking water, and residential exposures. In an aggregate assessment, exposures from relevant sources are added together and compared to quantitative estimates of hazard (e.g., a NOAEL or PAD), or the risks themselves can be aggregated. When aggregating exposures and risks from various sources, HED considers both the route and duration of exposure.

As previously noted, there are no residential uses for fluensulfone at this time; therefore, dietary (food and water) exposure is the only pathway appropriate for assessment. Aggregate risk estimates are equivalent to the dietary risk estimates discussed above and are not of concern.

Cumulative Risk

Unlike other pesticides for which EPA has followed a cumulative risk approach based on a common mechanism of toxicity, EPA has not made a common mechanism of toxicity finding as to fluensulfone and any other substances and fluensulfone does not appear to produce a toxic metabolite produced by other substances. For the purposes of this tolerance action, therefore, EPA has not assumed that fluensulfone has a common mechanism of toxicity with other substances. For information regarding EPA's efforts to determine which chemicals have a common mechanism of toxicity and to evaluate the cumulative effects of such chemicals, see the policy statements released by EPA's Office of Pesticide Programs concerning common mechanism determinations and procedures for cumulating effects from substances found to have a common mechanism on EPA's website at http://www.epa.gov/pesticides/cumulative/.

Attachments

1. Summary of OECD MRL/Tolerance Calculation Procedures
2. Inputs to the Acute Dietary Assessment
3. Inputs to the Chronic Dietary Assessment
4. Summary of the Acute Dietary Assessment Results
5. Summary of the Chronic Dietary Assessment Results

Attachment 1. Summary of OECD MRL/Tolerance Calculation Procedures

BSA as Fluensulfone
Carrot
USA
Preplant 2.5 lb ai/A

Total number of data (n)	12
Percentage of censored data	8%
Number of non-censored data	11
Lowest residue	0.010
Highest residue	1.204
Median residue	0.247
Mean	0.337
Standard deviation (SD)	0.335
Correction factor for censoring (CF)	0.944

Proposed MRL estimate

- Highest residue	1.204
- Mean + 4 SD	1.676
- CF x 3 Mean	0.955
Unrounded MRL	1.676
Rounded MRL	2

Residues (mg/kg)	n
< 0.01	1
0.059	1
0.091	1
0.130	1
0.184	1
0.217	1
0.276	1
0.336	1
0.371	1
0.457	1
0.708	1
1.20	1

Attachment 2. Inputs to the Acute Dietary Assessment

Filename: Acute Fluen PRZM-GW S18 separate.r08
Chemical: Fluensulfone Systemic
RfD(Chronic): .03 mg/kg bw/day NOEL(Chronic): 0 mg/kg bw/day
RfD(Acute): .18 mg/kg bw/day NOEL(Acute): 0 mg/kg bw/day
Date created/last modified: 05-29-2015/21:49:49 Program ver. 3.16, 03-08-d

EPA Code	Crop Grp	Commodity Name	Def Res (ppm)	Adj.Factors #1	Adj.Factors #2	Comment
0101078000	1AB	Carrot	0.500000	1.000	1.000	
0101078001	1AB	Carrot-babyfood	0.500000	1.000	1.000	
0101079000	1AB	Carrot, juice	0.500000	1.000	1.000	
0801374000	8A	Tomatillo	0.010000	1.000	1.000	
0801375000	8A	Tomato	0.010000	1.000	1.000	
0801375001	8A	Tomato-babyfood	0.010000	1.000	1.000	
0801376000	8A	Tomato, paste	0.010000	1.000	1.000	
0801376001	8A	Tomato, paste-babyfood	0.010000	1.000	1.000	
0801377000	8A	Tomato, puree	0.010000	1.000	1.000	
0801377001	8A	Tomato, puree-babyfood	0.010000	1.000	1.000	
0801378000	8A	Tomato, dried	0.010000	1.000	1.000	
0801378001	8A	Tomato, dried-babyfood	0.010000	1.000	1.000	
0801379000	8A	Tomato, juice	0.010000	1.000	1.000	
0801380000	8A	Tomato, Tree	0.010000	1.000	1.000	
0802148000	8BC	Eggplant	0.010000	1.000	1.000	
0802234000	8BC	Okra	0.010000	1.000	1.000	
0802270000	8B	Pepper, bell	0.010000	1.000	1.000	
0802270001	8B	Pepper, bell-babyfood	0.010000	1.000	1.000	
0802271000	8B	Pepper, bell, dried	0.010000	1.000	1.000	
0802271001	8B	Pepper, bell, dried-babyfood	0.010000	1.000	1.000	
0802272000	8BC	Pepper, nonbell	0.010000	1.000	1.000	
0802272001	8BC	Pepper, nonbell-babyfood	0.010000	1.000	1.000	
0802273000	8BC	Pepper, nonbell, dried	0.010000	1.000	1.000	
0901075000	9A	Cantaloupe	0.010000	1.000	1.000	
0901187000	9A	Honeydew melon	0.010000	1.000	1.000	
0901399000	9A	Watermelon	0.010000	1.000	1.000	
0901400000	9A	Watermelon, juice	0.010000	1.000	1.000	
0902021000	9B	Balsam pear	0.010000	1.000	1.000	
0902088000	9B	Chayote, fruit	0.010000	1.000	1.000	
0902102000	9B	Chinese waxgourd	0.010000	1.000	1.000	
0902135000	9B	Cucumber	0.010000	1.000	1.000	
0902308000	9B	Pumpkin	0.010000	1.000	1.000	
0902309000	9B	Pumpkin, seed	0.010000	1.000	1.000	
0902356000	9B	Squash, summer	0.010000	1.000	1.000	
0902356001	9B	Squash, summer-babyfood	0.010000	1.000	1.000	
0902357000	9B	Squash, winter	0.010000	1.000	1.000	
0902357001	9B	Squash, winter-babyfood	0.010000	1.000	1.000	
8601000000	86A	Water, direct, all sources	0.077600	1.000	1.000	
8602000000	86B	Water, indirect, all sources	0.077600	1.000	1.000	

Attachment 3. Inputs to the Chronic Dietary Assessment

```
Filename: Chronic Fluen PRZM-GW S18 separate.r08
Chemical: Fluensulfone Systemic
RfD(Chronic): .03 mg/kg bw/day  NOEL(Chronic): 0 mg/kg bw/day
RfD(Acute): .18 mg/kg bw/day  NOEL(Acute):  0 mg/kg bw/day
Date created/last modified: 05-29-2015/21:50:21      Program ver. 3.16, 03-08-d
```

EPA Code	Crop Grp	Commodity Name	Def Res (ppm)	Adj.Factors #1	#2	Comment
0101078000	1AB	Carrot	0.500000	1.000	1.000	
0101078001	1AB	Carrot-babyfood	0.500000	1.000	1.000	
0101079000	1AB	Carrot, juice	0.500000	1.000	1.000	
0801374000	8A	Tomatillo	0.010000	1.000	1.000	
0801375000	8A	Tomato	0.010000	1.000	1.000	
0801375001	8A	Tomato-babyfood	0.010000	1.000	1.000	
0801376000	8A	Tomato, paste	0.010000	1.000	1.000	
0801376001	8A	Tomato, paste-babyfood	0.010000	1.000	1.000	
0801377000	8A	Tomato, puree	0.010000	1.000	1.000	
0801377001	8A	Tomato, puree-babyfood	0.010000	1.000	1.000	
0801378000	8A	Tomato, dried	0.010000	1.000	1.000	
0801378001	8A	Tomato, dried-babyfood	0.010000	1.000	1.000	
0801379000	8A	Tomato, juice	0.010000	1.000	1.000	
0801380000	8A	Tomato, Tree	0.010000	1.000	1.000	
0802148000	8BC	Eggplant	0.010000	1.000	1.000	
0802234000	8BC	Okra	0.010000	1.000	1.000	
0802270000	8B	Pepper, bell	0.010000	1.000	1.000	
0802270001	8B	Pepper, bell-babyfood	0.010000	1.000	1.000	
0802271000	8B	Pepper, bell, dried	0.010000	1.000	1.000	
0802271001	8B	Pepper, bell, dried-babyfood	0.010000	1.000	1.000	
0802272000	8BC	Pepper, nonbell	0.010000	1.000	1.000	
0802272001	8BC	Pepper, nonbell-babyfood	0.010000	1.000	1.000	
0802273000	8BC	Pepper, nonbell, dried	0.010000	1.000	1.000	
0901075000	9A	Cantaloupe	0.010000	1.000	1.000	
0901187000	9A	Honeydew melon	0.010000	1.000	1.000	
0901399000	9A	Watermelon	0.010000	1.000	1.000	
0901400000	9A	Watermelon, juice	0.010000	1.000	1.000	
0902021000	9B	Balsam pear	0.010000	1.000	1.000	
0902088000	9B	Chayote, fruit	0.010000	1.000	1.000	
0902102000	9B	Chinese waxgourd	0.010000	1.000	1.000	
0902135000	9B	Cucumber	0.010000	1.000	1.000	
0902308000	9B	Pumpkin	0.010000	1.000	1.000	
0902309000	9B	Pumpkin, seed	0.010000	1.000	1.000	
0902356000	9B	Squash, summer	0.010000	1.000	1.000	
0902356001	9B	Squash, summer-babyfood	0.010000	1.000	1.000	
0902357000	9B	Squash, winter	0.010000	1.000	1.000	
0902357001	9B	Squash, winter-babyfood	0.010000	1.000	1.000	
8601000000	86A	Water, direct, all sources	0.052500	1.000	1.000	
8602000000	86B	Water, indirect, all sources	0.052500	1.000	1.000	

Attachment 4. Summary of the Acute Dietary Assessment Results

```
OPP Health Effects Division                                    Ver. 3.16, 03-08-d
DEEM-FCID ACUTE Analysis for FLUENSULFONE SYSTEMIC          NHANES 2003-2008 2-Day
Residue file: Acute Fluen PRZM-GW S18 separate.r08
Adjustment factor #2 NOT used.
Analysis Date: 05-29-2015/21:52:50    Residue file dated: 05-29-2015/21:49:49
RAC/FF intake summed over 24 hours
Run Comment: ""
===============================================================================
```

Summary calculations--per capita:

	95th Percentile		99th Percentile		99.9th Percentile	
	Exposure	% aRfD	Exposure	% aRfD	Exposure	% aRfD
Total US Population:	0.004466	2.48	0.007375	4.10	0.013782	7.66
All Infants:	0.013766	7.65	0.019161	10.65	0.026334	14.63
Children 1-2:	0.007188	3.99	0.011105	6.17	0.024770	13.76
Children 3-5:	0.005774	3.21	0.008336	4.63	0.013205	7.34
Children 6-12:	0.004210	2.34	0.007023	3.90	0.010497	5.83
Youth 13-19:	0.003600	2.00	0.005865	3.26	0.008811	4.89
Adults 20-49:	0.004267	2.37	0.006300	3.50	0.009049	5.03
Adults 50-99:	0.003862	2.15	0.005791	3.22	0.008845	4.91
Female 13-49:	0.004329	2.41	0.006373	3.54	0.008770	4.87

Attachment 5. Summary of the Chronic Dietary Assessment Results

```
OPP Health Effects Division                                      Ver. 3.16, 03-08-d
DEEM-FCID Chronic analysis for FLUENSULFONE SYSTEMIC         NHANES 2003-2008 2-day
Residue file name: Chronic Fluen PRZM-GW S18 separate.r08
                                                    Adjustment factor #2 NOT used.
Analysis Date 05-29-2015/21:51:32     Residue file dated: 05-29-2015/21:50:21
Reference dose (RfD, Chronic) = .03 mg/kg bw/day
===============================================================================
                    Total exposure by population subgroup
-------------------------------------------------------------------------------
```

Population Subgroup	Total Exposure mg/kg body wt/day	Percent of Rfd
Total US Population	0.001195	4.0%
Hispanic	0.001155	3.8%
Non-Hisp-White	0.001227	4.1%
Non-Hisp-Black	0.000970	3.2%
Non-Hisp-Other	0.001411	4.7%
Nursing Infants	0.001452	4.8%
Non-Nursing Infants	0.004293	14.3%
Female 13+ PREG	0.001097	3.7%
Children 1-6	0.001658	5.5%
Children 7-12	0.001027	3.4%
Male 13-19	0.000812	2.7%
Female 13-19/NP	0.000901	3.0%
Male 20+	0.001090	3.6%
Female 20+/NP	0.001233	4.1%
Seniors 55+	0.001143	3.8%
All Infants	0.003416	11.4%
Female 13-50	0.001164	3.9%
Children 1-2	0.001921	6.4%
Children 3-5	0.001549	5.2%
Children 6-12	0.001084	3.6%
Youth 13-19	0.000857	2.9%
Adults 20-49	0.001166	3.9%
Adults 50-99	0.001161	3.9%
Female 13-49	0.001163	3.9%

Appendix 5: Journal of Nematology Article

Ploeg, A.; Stoddard, S. and Becker, J.O. (2019). Control of Meloidoyme incognita is sweetpotato with fluensulfone. Journal of Nematology (51): 1-8p.

exeley

JOURNAL OF NEMATOLOGY

Article | DOI: 10.21307/jofnem-2019-018

e2019-18 | Vol. 51

Control of *Meloidogyne incognita* in sweetpotato with fluensulfone

Antoon Ploeg[1], Scott Stoddard[2], and J. Ole Becker[1]

[1]Department of Nematology, University of California Riverside, 3401 Watkins drive, Riverside, CA, 92521.

[2]UCCE Merced and Madera Counties, 2145 Wardrobe Ave, Merced, CA, 95341.

E-mail: antoon.ploeg@ucr.edu

This paper was edited by Horacio Lopez-Nicora.

Received for publication September 17, 2018.

Abstract

In California, sweetpotato is mostly grown on light sandy soils in Merced County. Root-knot nematodes (*Meloidogyne* spp.) can reduce sweetpotato yields and quality. Fluensulfone is the active ingredient of the new non-fumigant nematicide Nimitz. Unlike fumigant nematicides, toxicity toward non-target organisms is low, and it does not emit volatile organic compounds which negatively impact air quality. In two field trials, the effect of fluensulfone on *M. incognita* levels, and on the yield and quality of sweetpotato was determined. Fluensulfone was applied as a pre-plant soil incorporated drench or as a drench followed by post-plant sprays. Fluensulfone treatments more than doubled the marketable yields over an untreated control and a metam-sodium treatment in both trials. It strongly reduced nematode symptoms on the harvested roots and nematode infestation of these roots. The lowest rate of fluensulfone was as effective as the higher rates, and post-plant sprays following a pre-plant soil incorporated drench did not result in any additional benefits. Fluensulfone did not reduce soil nematode levels at harvest. It was concluded that a pre-plant incorporated fluensulfone drench at a rate of 1.96 kg/ha could provide a viable alternative for currently used nematicides to mitigate root-knot nematode damage in sweetpotato.

Key words

Fluensulfone, *Ipomea batatas, Meloidogyne incognita*, Management, Nimitz, Sweetpotato.

Sweetpotato (*Ipomea batatas*) production in California was approximately 295 million kg annually during 2010 to 2015 grown on approximately 7,300 ha. California production is second only to North Carolina, and the crop in California is valued at $150 million, which is about 20% of the total US value. Close to 90% of the production in California is concentrated on the sandy soils of Merced County in the San Joaquin Valley (USDA/NASS). Planting material is typically produced in plastic tunnels (hotbeds) by planting sweetpotato roots from the previous year. After sprouting, the stems are cut, and these stem cuttings or ‘slips’ which do not have any roots, are used as planting material in April to May in the production fields (about 37,000 slips per hectare) (Stoddard et al., 2013). In California production fields, the crop is usually grown in double rows on 203 cm-wide (center to center) beds, and irrigation is through surface drip tubing on the center of the bed (Stoddard et al., 2013).

Root-knot nematodes (RKN: *Meloidogyne* spp.) are economically the most damaging nematodes in sweetpotato both on a worldwide scale as well as in California (Overstreet, 2009). Crop loss estimates of 10% due to RKN were reported in California (Koenning et al., 1999). Unlike many other vegetable crops, most sweetpotato cultivars are particularly sensitive to RKN damage because symptoms develop directly on the harvested product. Symptoms of RKN on the harvested storage roots depend on the sweetpotato cultivar but generally include blistering or bumpiness of the storage root surface (Overstreet, 2009). Some cultivars may exhibit cracking of the storage roots. Lawrence et al. (1986) suggested that RKN predispose the roots to cracking when soil moisture levels fluctuate during the development of the storage roots, rather than directly causing this symptom. Generally, RKN females and egg masses are easily found embedded in the storage roots just below the surface and may be associated with pinpoint necrotic spots (Lawrence et al., 1986). Apart from a reduction in quality, a general reduction in yield (kg/ha) is also common (Roberts and Scheuerman, 1984; Overstreet, 2009). Economic damage thresholds for the RKN species *M. incognita* depend on the cultivar and environmental factors, but Ferris (1978) reported a threshold level of 5 s-stage juveniles (J2) per 1 kg soil for a sandy soil. Lawrence et al. (1986) found a damage threshold of 10 J2 per 500 cm^3 soil for cracking of storage roots. Overstreet (2009) and Stoddard et al. (2013) also hint at very low threshold levels.

Some cultivars (e.g. Covington, Murasaki) have good RKN resistance, but under high soil temperatures, even resistant cultivars can still result in a large RKN population increase during one crop cycle (Roberts and Scheuerman, 1984). Furthermore, although storage root quality of resistant cultivars was not affected by RKN, yield losses resulting from RKN were still considerable, and additional management strategies are needed in RKN infested fields, even when growing RKN-resistant cultivars (Roberts and Scheuerman, 1984).

Typically soil fumigants are used to control RKN both in nursery hotbeds and in production fields. According to 2015 data (CA-DPR), sweetpotato was among the five crops in California with the highest use of the fumigant 1,3-dichloropropene (2,999 ha). Other fumigants used in sweetpotato in California are metam-potassium (809 ha) and metam-sodium (33 ha). As they are potential environmental and health hazards, they are limited by regulatory restrictions related to the emission of volatile organic compounds (VOC) and their toxicity. Until recently, effective, environmentally acceptable, and economically viable alternatives were not available, and this has been an important factor in the continued use of soil fumigants (Noling and Becker, 1994; Becker, 2014). Fluensulfone (tradename: Nimitz, ADAMA Agricultural Solutions Ltd., Raleigh, NC) is a non-fumigant nematicide that is registered for use in fruiting vegetable crops in California. It has a 'caution' label and no re-entry interval (0 hr REI) after application. The product is applied pre-plant, either by chemigation through the drip tubing, or by soil incorporation at rates between 4.1 and 5.8 liter/ha (www.adama.com). Studies on RKN control by fluensulfone in tomato, carrot, tobacco, and cucumber showed promising results (Csinos et al., 2010; Becker et al., 2013; Dickson and Mendes, 2013; Ploeg et al., 2013; Morris et al., 2015, 2016). Although Dickson and Mendes (2013) mention a yield increase in sweetpotato after a fluensulfone application, they do not provide further information.

The goal of this two-year field study was to evaluate the effectiveness of fluensulfone in comparison to an untreated control and to metam-sodium in sweetpotato grown on an uniformly *M. incognita*-infested site.

Materials and methods

The trials were located on a field with sandy-loam soil (70% sand, 18% silt, 12% clay, 0.1% organic matter, pH 7.3) at the University of California South Coast Research and Extension Center, Irvine, CA. The field had been inoculated five years previously with an egg suspension of a *M. incognita* race 3 population, originally isolated from cotton in the San Joaquin Valley, CA, by injecting the egg suspension through buried drip tubing (Becker et al., 1989). The *M. incognita*-susceptible crops melon (*Cucumis melo* 'Durango'), carrot (*Daucus carota* 'Imperator 58'), tomato (*Solanum lycopersicum* 'Halley 3155'), and bean (*Phaseolus vulgaris* 'Blue Lake 274') were grown in sequence during the spring/summer for four years to increase and maintain an evenly distributed *M. incognita* infestation level before the sweetpotato trial was initiated. Wheat (*Triticum aestivum*) 'Yecora Rojo' was grown during the winter each year.

The trials were conducted in 2016 and 2017 on different, but nearby areas of the field. In both years, 152 cm wide (center to center) beds were prepared in May and plots were laid out. Individual plots were 6.1 m long sections of bed, separated along the beds by a 91 cm border section. The experiment was designed according to a completely randomized block design with five replicates and four treatments. In both years treatments included an untreated control, a Vapam (a.i. metam-sodium) treatment at 701 liter/ha (294 liter a.i./ha), and two fluensulfone treatments. In 2016, the fluensulfone treatments were (i) Nimitz at 7 liter/ha (3.36 kg a.i./ha, pre-plant incorporated) and (ii) Nimitz at 7 liter/ha (3.36 kg a.i./ha, pre-plant incorporated) followed by two post-plant spray applications of 3.5 liter/ha (1.68 kg a.i./ha) at 26 and 58 d after planting. In 2017, fluensulfone treatments were (i) Nimitz at 5.8 liter/ha (2.8 kg a.i./ha) and (ii) Nimitz at 4.1 liter/ha (1.96 kg a.i./ha) both pre-plant incorporated. Vapam was applied 21 and 26 d before planting in 2016 and

2017, respectively. Pre-plant Nimitz applications were 2 and 7 d before planting in 2016 and 2017, respectively. Amounts applied per plot were based on the bed surface area of each plot (5.88 m^2). All plots were pre-irrigated for 1 hr with overhead sprinklers the day prior to any pre-plant application to achieve adequate soil moisture. For each plot, Vapam and pre-plant Nimitz were suspended in 7.6 liter of water and watered evenly over the plot surface with a watering can. An additional 45.4 liter of water was applied over each plot, and the plots were tilled with a rototiller to a depth of 10 to 13 cm. Post-plant Nimitz applications were applied in 7.6 liter of water with a backpack sprayer over the crop foliage.

For RKN analysis, a composite sample consisting of six cores of soil (1.5 cm diameter, 5–30 cm depth) was collected from each plot just before applying Vapam (initial population: Pi) and just before harvest (final population: Pf). Nematodes were extracted from 100 g soil subsamples in a modified Baerman-funnel technique (Rodriguez-Kabana and Pope, 1981), and RKN J2 were counted at ×40 magnification.

Rootless slips of the RKN-susceptible cultivars O'Henry and Beauregard were planted on June 10, 2016 and May 18, 2017, respectively. The slips were planted in pre-wetted beds at 41 cm within-row spacing, with two rows per bed, resulting in 30 slips per plot. At planting, approximately 0.5 liter water was added to each cutting, and irrigation was through drip tubing (drip emitters 2 liter/hr, 30.5 cm spacing) on top and in the center of the beds. Fertilization was according to standard practices, applied pre-plant incorporated and post-plant through the drip tubing. Weeds were removed by hand, and no fungicides or insecticides were required. In total, 20 and 50 d after planting, the general vigor of each plot was visually examined and indexed (1–10 scale). Plots were harvested mechanically on October 9, 2016 and September 22, 2017. For each plot, total yields (weight and number of roots) were determined. In total, 20 roots were randomly collected from each plot, and assigned to one of three categories: marketable, non-marketable because of RKN damage, and non-marketable because of defects not related to RKN. The weight of these roots in each category was determined. In addition, 10 randomly selected roots from each plot were taken to the laboratory and cut in half crosswise. One half was discarded. The 10 remaining half

Table 1. Average ($n=5$) vigor of sweetpotato cultivars O'Henry (2016) and Beauregard (2017) in four treatments 20 and 50 d post-plant. Field located at SCREC, Irvine, CA[1]. Vigor rating from 1 to 10 (very poor — excellent) ± standard error.

	Vigor rating (days after planting)	
Treatment	20	50
2016		
1. Untreated Control	7.4 ± 0.89	7.2 ± 0.84
2. Metam-sodium (294 liter/ha)	8.0 ± 0.71	7.8 ± 0.45
3. Fluensulfone pre-plant (3.36 kg/ha)	7.6 ± 0.89	7.6 ± 0.55
4. Fluensulfone pre-plant (3.36 kg/ha) and 2× post (1.68 kg/ha + 1.68 kg/ha)	7.8 ± 0.45	7.6 ± 0.55
treatment *P-value*	0.62	0.56
2017		
1. Untreated Control	4.8 ± 0.49	6.0 ± 0.32
2. Metam-sodium (294 liter/ha)	6.0 ± 0.89	6.2 ± 0.37
3. Fluensulfone pre-plant (1.96 kg/ha)	7.2 ± 0.66	7.2 ± 0.37
4. Fluensulfone pre-plant (2.8 kg/ha)	6.4 ± 0.81	6.4 ± 0.40
Treatment *P-value*	0.19	0.20

Notes: [a]Plot size: 6.1 m long section of 152-cm wide beds. Two lines of sweetpotato planted per bed.

roots were weighed and then peeled with a potato peeler. Nematode eggs were extracted from both the peels and the peeled roots by shaking for 3 min in a 0.5% NaOCl solution (Hussey and Barker, 1973) and collected by washing over two stacked 25 µm pore-size sieves. The eggs were counted at ×40 magnification.

Statistical analysis

Treatment effects on nematode counts, crop vigor, sweetpotato yield, and sweetpotato quality were analyzed using an analysis of variance (ANOVA) procedure, and means were compared using Fisher's protected least significant difference (LSD) test ($P \leqslant 0.05$) using SAS statistical software (SAS Institute, Cary, NC, USA). Percentage data were transformed by arcsin ($\sqrt{x}$) before statistical analysis, nematode counts were transformed by $x^1 = \log_{10}(x+1)$ before statistical analysis.

Results

General growing conditions for the trial were excellent in both years, and nearly 100% of planted slips survived. In both trial years, crop vigor was not affected by the treatments (Table 1). In 2016, effects of the two fluensulfone treatments on sweetpotato yields (kg) were highly significant. Both fluensulfone treatments more than doubled the overall yield relative to the untreated control (Table 2). In 2017, the fluensulfone treatments yielded about 9 kg/plot more than the untreated controls, but these differences were not significant. In both years, the fluensulfone treatments dramatically increased the marketable yield compared to the untreated control. The metam-sodium treatment failed to improve sweetpotato yields (quantity, quality) and was not significantly better than the untreated control. When examining the yields as percentages from the total yield, the same general effects exist (Table 3). Compared to the untreated

Table 2. Average yield ($n=5$ ± standard error) of harvested sweetpotato after four treatments assigned to three categories, market (marketable size and quality), cull RKN (culled because of root-knot nematode damage), and cull other (culled because of non-nematode causes). Field trials were conducted during 2016 (cultivar O'Henry) and 2017 (cultivar Beauregard) at SCREC, Irvine, CA[1].

	Sweetpotato Yield (kg/plot[a])							
Treatment	Total		Market		Cull RKN		Cull other	
2016								
1. Untreated Control	14.9 ± 1.5	b[b]	0.8 ± 0.4	b	10.5 ± 1.5	a	3.6 ± 1.2	b
2. Metam-sodium (294 liter/ha)	19.7 ± 5.0	b	0.9 ± 0.3	b	11.7 ± 1.5	a	7.0 ± 3.5	b
3. Fluensulfone pre-plant (3.36 kg/ha)	29.6 ± 3.5	a	8.2 ± 0.2	a	4.6 ± 1.3	b	16.8 ± 3.0	a
4. Fluensulfone pre-plant (3.36 kg/ha) and 2× post (1.68 kg/ha + 1.68 kg/ha)	29.8 ± 3.0	a	10.1 ± 0.4	a	3.6 ± 0.7	b	16.1 ± 2.6	a
Treatment *P*-value	0.01		0.0001		0.0003		0.006	
2017								
1. Untreated Control	24.8 ± 2.7	a	6.7 ± 1.9	b	15.0 ± 3.9	a	3.1 ± 0.6	a
2. Metam-sodium (294 liter/ha)	27.7 ± 2.8	a	9.9 ± 1.0	b	12.5 ± 2.7	a	5.3 ± 1.2	a
3. Fluensulfone pre-plant (1.96 kg/ha)	34.0 ± 2.4	a	18.4 ± 2.6	a	12.0 ± 2.6	a	3.5 ± 1.4	a
4. Fluensulfone pre-plant (2.8 kg/ha)	33.0 ± 3.6	a	23.3 ± 3.4	a	7.1 ± 1.4	a	2.6 ± 0.8	a
Treatment *P-value*	0.13		0.002		0.32		0.30	

Notes: [a]Plot size: 6.1 m long section of 152-cm wide beds. Two lines of sweetpotato planted per bed; [b]different letters within the same column and within the same year represent significant differences at the 95% confidence level.

Table 3. Average percentage ($n=5$ ± standard error) of harvested sweetpotato after four treatments assigned to three categories, market: marketable root size and quality, cull RKN: culled because of root-knot nematode damage, and cull other: culled because of non-nematode causes. Field trials during 2016 (cultivar 'O'Henry') and 2017 (cultivar 'Beauregard') at SCREC, Irvine, CA.

	Sweetpotato yield (%)					
Treatment	Market		Cull RKN		Cull other	
2016						
1. Untreated Control	6.6 ± 4.3	b[a]	70.3 ± 8.1	a	23.3 ± 6.0	b
2. Metam-sodium (294 liter/ha)	5.3 ± 2.3	b	66.3 ± 6.9	a	28.5 ± 7.4	b
3. Fluensulfone pre-plant (3.36 kg/ha)	28.3 ± 5.3	a	16.4 ± 5.5	b	55.4 ± 3.8	a
4. Fluensulfone pre-plant (3.36 kg/ha) and 2× post (1.68 kg/ha + 1.68 kg/ha)	35.1 ± 2.9	a	12.0 ± 2.1	b	53.0 ± 4.3	a
Treatment *P-value*	0.0001		0.0043		0.003	
2017						
1. Untreated Control	29 ± 8.0	c	58 ± 9.4	a	13 ± 3.0	a
2. Metam-sodium (294 liter/ha)	37 ± 4.0	bc	44 ± 7.0	ab	19 ± 4.3	a
3. Fluensulfone pre-plant (1.96 kg/ha)	54 ± 6.6	ab	35 ± 7.6	bc	11 ± 5.1	a
4. Fluensulfone pre-plant (2.8 kg/ha)	70 ± 3.2	a	21 ± 2.9	c	9 ± 2.9	a
Treatment *P-value*	0.005		0.02		0.27	

Notes: [a]Different letters within the same column and within the same year represent significant differences at the 95% confidence level. Data were transformed by arcsin [√(x/100)] before statistical analysis, non-transformed data shown.

control, the percentage of harvested roots culled because of obvious RKN symptoms (bumpiness, cracking) was reduced by the fluensulfone treatments in both years. In 2016, the percentage of roots culled because of other reasons (insect damage, too small, misshapen) was significantly higher in both fluensulfone treatments, but this was not the case in 2017. Metam-sodium treatments did not significantly affect the relative tuber yields in the three different quality classes (marketable, cull RKN, cull other) compared to the untreated control in either year.

The average RKN J2 levels at the start of the trial were 15.8 and 47.5 J2 per 100 g soil in 2016 and 2017, respectively (Table 4). In both years, these pre-treatment nematode levels were not significantly different among the treatments. At harvest, nematode levels had increased about 13-fold in 2016 and 8-fold in 2017 and were not significantly different among the four treatments. In both years, the level of nematode infestation of the harvested sweetpotato roots however was significantly lowered by the fluensulfone treatments resulting in a reduction of the egg load of the roots by over 80% compared to the untreated control. The metam-sodium treatment did not result in a significant reduction in sweetpotato root infestation levels at harvest relative to the untreated control.

Discussion

The earliest report of fluensulfone use against nematodes was from 2010 showing that the nematicide reduced root-galling and increased yield of tobacco grown in a *M. arenaria* infested site (Csinos et al., 2010). Since then, most studies on the use and efficacy of fluensulfone for nematode control have been done on fruiting vegetables. The registration of Nimitz (a.i. fluensulfone) in the USA was first obtained for these crops (Gine, 2016). Current registration also includes leafy vegetables, brassica vegetables, and

Table 4. Average root-knot nematode levels ($n=5$ ± standard error) in soil and on harvested sweetpotato after four treatments. Field trials during 2016 (cultivar O'Henry) and 2017 (cultivar Beauregard) at SCREC, Irvine, CA.

	J2 per 100 g soil					
Treatment	Pre-plant (Pi)		Post-plant (Pf)		Eggs per g sweetpotato	
2016						
1. Untreated Control	23 ± 16	a[a]	198 ± 42	a	536 ± 38	a
2. Metam-sodium (294 liter/ha)	12 ± 5	a	300 ± 61	a	573 ± 133	a
3. Fluensulfone pre-plant (3.36 kg/ha)	14 ± 6		173 ± 51	a	79 ± 17	b
4. Fluensulfone pre-plant (3.36 kg/ha) and 2x post (1.68 kg/ha + 1.68 kg/ha)	14 ± 8	a	156 ± 33	a	98 ± 34	b
Treatment *P-value*	0.95		0.29		0.0001	
2017						
1. Untreated Control	21.2 ± 9.1	a	360 ± 107	a	304 ± 46	a
2. Metam-sodium (294 liter/ha)	25.0 ± 12.3	a	261 ± 52	a	228 ± 87	a
3. Fluensulfone pre-plant (1.96 kg/ha)	34.4 ± 14.4	a	396 ± 80	a	37 ± 16	b
4. Fluensulfone pre-plant (2.8 kg/ha)	49.0 ± 17.8	a	532 ± 132	a	21 ± 5	b
Treatment *P-value*	0.65		0.54		0.0005	

Notes: [a]Different letters within the same column and within the same year represent significant differences at the 95% confidence level. Data were transformed by arcsin [√(x/100)] before statistical analysis, non-transformed data shown.

strawberry. The efficacy of fluensulfone in root and tuber crops was also being tested such as in carrot (Ploeg et al., 2013; Westerdahl, 2014), potato (Norshie et al., 2016), and sweetpotato in this study. In these crops, the adverse impact of nematodes on the quality of the harvested product is often more significant than the impact on overall yield. In both years in our study, pre-plant nematode levels were at least 15 J2/100 g soil, which corresponds to approximately 120 J2/500 cm^3. Because damage thresholds are estimated at only 10 J2/500 cm^3, it is not surprising that in both years over 50% percent of roots were culled in the untreated control. Fluensulfone treatments increased the percentage of marketable sweetpotatoes in both years over the untreated control, but within the same year, fluensulfone treatments were not different. This indicates that post-plant spray applications did not provide an additional benefit after a pre-plant soil incorporated treatment (2016) and that a pre-plant soil incorporated rate of fluensulfone at 1.96 kg/ha was as effective as the 2.8 kg/ha rate (2017). Surprisingly, in 2016 the percentage of culled roots that did not show obvious signs of nematode damage (bumpy appearance, cracking) was significantly higher after the two fluensulfone treatments. This suggests that fluensulfone caused some other effect on the roots, e.g., increased the number of roots with insect damage, or resulted in more misshapen or small roots. An increase in insect (wireworm) damaged roots resulting from fluensulfone seems unlikely, but it could be that in 2016 Nimitz did reduce nematode symptoms of the roots, but at the same time had some phytotoxic effect resulting in more misshapen and smaller roots. This would explain the relatively higher percentage of 'no-nematode' culls in the fluensulfone treatments in 2016. In 2017, when lower rates were used, this effect did not occur. Phytotoxic effects of fluensulfone in vegetable crops have been reported when used at high rates, as a post-plant spray, or too close to planting time (Oka et al., 2012; Van Dyk et al., 2013; Morris et al., 2016). Stoddard (2010) observed early-season phytotoxic effects associated with

MCW-2 (a.i. fluensulfone) treatments in a California sweetpotato field trial.

In both years, the RKN J2 soil populations at harvest were similar among the treatments. This was true also in previous field trials on carrot (Ploeg et al., 2013) and tomato (Becker et al., 2013), although others did find that fluensulfone resulted in significant reductions in RKN J2 populations at harvest in field or microplot trials with tobacco (Csinos et al., 2010), tomato (Morris et al., 2015), and lima bean (Jones et al., 2017). In our trials, the metam-sodium treatment did not differ from the untreated control. This may have been due to the relatively superficial incorporation of the product and the failure to provide an adequate seal post application. The positive effect of fluensulfone on the marketable root yield was reflected in its ability to strongly reduce nematode infestation of the harvested storage roots, even though soil RKN populations were not lowered. This suggests that nematode infestation of the storage roots was more effectively controlled than of the feeder roots and that the increase in nematode soil levels in the fluensulfone treatments was mostly the result of nematode multiplication in the feeder roots. Possibly, the developing young storage roots are most susceptible to RKN infestation, when the activity of fluensulfone is still high, and lose their susceptibility as they develop, while the feeder roots remain susceptible throughout the crop cycle. The observed outcome is similar to what Roberts and Scheuerman (1984) observed after growing nematode resistant sweetpotato cultivars: the storage roots remained virtually free of nematode symptoms while post-harvest soil RKN populations increased. Villordon et al. (2009) noted that storage root development in sweetpotato is largely determined in the first 17 d after transplanting.

These trials show that fluensulfone when applied as an incorporated soil drench at least 2 d before planting a nematode-susceptible sweetpotato cultivar in RKN (*M. incognita*) infested soil, significantly improves both yield and quality. Total root yields doubled, and a 10-fold increase in marketable yield occurred compared to the untreated control. The 1.96 kg/ha rate was as effective as the 2.8 kg/ha rate, and post-plant spray applications did not offer additional benefits. However, this lower rate will need to be evaluated in additional field trials before it can be recommended to sweetpotato producers. Fluensulfone failed to reduce soil RKN levels at harvest time but did reduce nematode infestation of sweetpotato roots by over 80%. We conclude that fluensulfone provides a viable new management option to growers in California for reducing RKN damage in sweetpotato that is both safe and effective.

Acknowledgments

The authors wish to thank Scott Edwards, Angelo Loffredo, and personnel of the ANR South Coast Research and Extension Center, Irvine, CA for technical support.

References

Becker, J. O. 2014. Plant health management: crop protection with nematicides in VanAlfen, N. (Ed.), Encyclopedia of agriculture and food systems 4, Elsevier, San Diego, CA: 400–7.

Becker, J. O., Ploeg, A. and Nunez, J. 2013. Efficacy of nematicides for root-knot nematode management in tomato 2012. Plant Disease Management Report 7:N009. Online publication. https://10.1094/PDMR07.

Becker, J. O., Monson, M., Van Gundy, S. D. and Schroth, M. N. 1989. Drip irrigation as a delivery system for infestation of field plots with nematodes. Journal of Nematology 21:524–9.

Csinos, A., Whitehead, J., Hickman, L. and LaHue, S. S. 2010. Evaluation of fluensulfone for root-knot nematode on tobacco. Phytopathology 100 (supplement), Page S28.

Dickson, D. W. and Mendes, M. L. 2013. Efficacy of MCW-2 on Florida vegetables. Journal of Nematology 45:287–8.

Ferris, H. 1978. Development of nematode damage functions and economic thresholds using *Meloidogyne incognita* on tomatoes and sweetpotatoes. Journal of Nematology 10:286.

Gine, N. P. A. 2016. New non-fumigant contact nematicide Nimitz®, update on new coming label. Journal of Nematology 48:355–6.

Hussey, R. S. and Barker, K. R. 1973. A comparison of methods of collecting inocula for *Meloidogyne* spp., including a new technique. Plant Disease Reporter 57:1025–8.

Jones, J. G., Kleczewski, N. M., Desaeger, J., Meyer, S. L. F., and Johnson, G. C. 2017. Evaluation of nematicides for southern root-knot nematode management in lima bean. Crop Protection 96:151–7.

Koenning, S. R., Overstreet, C., Noling, J. W., Donald, P. A., Becker, J. O. and Fortnum, B. A. 1999. Survey of crop losses in response to phytoparasitic nematodes in the United States for 1994. Journal of Nematology 31:587–618.

Lawrence, G. W., Clark, C. A. and Wright, V. L. 1986. Influence of *Meloidogyne incognita* on resistant and susceptible sweetpotato cultivars. Journal of Nematology 18:59–65.

Morris, K. A., Langston, D. B., Davis, R. F., Noe, J. P., Dickson, D. W. and Timper, P. 2016. Efficacy of various application methods of fluensulfone for managing root-knot nematodes in vegetables. Journal of Nematology 48:65–71.

Morris, K. A., Langston, D. B., Dickson, D. W., Davis, R. F., Timper, P. and Noe, J. P. 2015. Efficacy of fluensulfone in a tomato–cucumber double cropping system. Journal of Nematology 47:310–5.

Noling, J. W. and Becker, J. O. 1994. The challenge of research and extension to define and implement alternatives to methyl bromide. Journal of Nematology 26:573–86.

Norshie, P. M., Grove, I. G. and Back, M. A. 2016. Field evaluation of the nematicide fluensulfone for control of the potato cyst nematode *Globodera pallida*. Pest Management Science 72:2001–7.

Oka, Y., Shuker, S. and Tkachi, N. 2012. Systemic nematicidal activity of fluensulfone against the root-knot nematode *Meloidogyne incognita* on pepper. Pest Management Science 68:268–75.

Overstreet, C. 2009. Nematodes in Loebenstein, G. and Thottappilly, G. (Eds), The sweetpotato Springer, Dordrecht: 135–59.

Ploeg, A., Becker, J. O. and Nunez, J. 2013. Efficacy of nematicides for root-knot nematode management in carrot 2012. Plant Disease Management Report 7 p. N021, doi: 10.1094/PDMR07.

Roberts, P. A., and Scheuerman, R. W. 1984. Field evaluations of sweetpotato clones for reaction to root-knot and stubby root nematodes in California. HortScience 19:270–3.

Stoddard, C. S., Davis, M. R. and Cantwell, M. 2013. Sweetpotato production in California. University of California Agriculture and Natural Resources (UC ANR) publication 7237, pp. 6.

Stoddard, S. 2010. Sweetpotato research progress report 2010. (August 14, 2018). pp. 26, available at: http://cemerced.ucanr.edu/files/139314.pdf.

Van Dyk, D., Jordan, K., and McDonald, M. R. 2013. Evaluating nematicides for the control of soil-borne nematode pests on vegetable crops in Ontario. (August 14, 2018). 36th International Carrot Conference. Madison, WI, August 15–16, 2013. Online publication: https://vcru.wisc.edu/simonlab/carrotconference/abstracts/402.htm.

Villordon, A. Q., La Bonte, D. R., Firon, N., Kfir, Y., Pressman, E. and Schwartz, A. 2009. Characterization of adventitious root development in sweetpotato. HortScience 44:651–5.

Westerdahl, B. 2014. Nimitz (MCW-2) for management of root-knot nematode on annual crops. Acta Horticulturae 1044:353–8.

Appendix 6: Agronomy Article

M. Kawanobe; K. Toyota; T. Fujita and D. Hatta. 2019. Evaluation of Nematicidal Activity of Fluensulfone against Non-Target Free-Living Nematodes under Field Conditions. Agronomy (9): 1 – 16p.

agronomy

MDPI

Article

Evaluation of Nematicidal Activity of Fluensulfone against Non-Target Free-Living Nematodes under Field Conditions

Masanori Kawanobe [1,2,*], Koki Toyota [1], Tomonori Fujita [1] and Daisuke Hatta [3]

1 Graduate School of Bio-Applications and Systems Engineering, Tokyo University of Agriculture and Technology, Koganei, Tokyo 184-8588, Japan; kokit@cc.tuat.ac.jp (K.T.); tomonorifujita998@gmail.com (T.F.)
2 Agri-RAND, Bunkyo-ku, Tokyo 113-0022, Japan
3 ADAMA JAPAN K.K., Minato-ku, Tokyo 105-0003, Japan; daisuke.hatta@adama.com
* Correspondence: masanori.kawanobe@jp-kawanobe.com; Tel.: +81-3-5834-0092

Received: 16 November 2019; Accepted: 2 December 2019; Published: 5 December 2019

check for updates

Abstract: The use of nematicides with reduced toxic side-effects against non-target free-living nematodes is a favorable option for farmers to control plant-parasitic nematodes. The nematicide fluensulfone was registered in several countries for the control of the root-knot nematodes, *Meloidogyne* spp. among other plant-parasitic nematodes. This study aimed to evaluate the nematicidal activity of fluensulfone against non-target nematode fauna in four field experiments, each under different conditions (soils types and plant hosts). Nematodes extracted from soil samples were classified and counted based on their morphological characters. Fluensulfone significantly reduced damage caused by root-knot nematodes to tomato and sweet potato plants, while overall non-target free-living nematode population densities were maintained at the same level as those in control. Different diversity indices (e.g., Shannon-Wiener *H'*, Simpson's *D*, species richness, evenness *J'*, maturity indices) and principal component analyses in the four experiments showed that fluensulfone treatment kept a similar diversity level of non-target free-living nematode fauna to that of the non-treated control. The results suggested that fluensulfone may have minimal impact to free-living nematode fauna in both population density and diversity when the nematicide was applied to control *Meloidogyne* spp.

Keywords: agroecosystem; biodiversity; fluensulfone; fosthiazate; free-living nematode; nematicide; non-target nematodes; 1,3-dichloropropene

1. Introduction

Soil biota consists of a wide variety of living organisms, both visible and microscopic; from plants, insects, amphibians, reptiles and mammals, to bacteria, fungi and nematodes. Farmlands are not an exception. Biodiversity on farmland is a precondition for sustainable farming [1]. Among soil organisms, nematodes play important roles in soil ecosystem function, such as nutrient cycling, decomposition and disease suppression [2]. Feeding activities of free-living nematodes generally lead to an increase in nutrient availability as a result of increased soil microbial activity and excretion of excess ingested nutrients [3], especially nitrogen mineralization [4,5]. Free-living nematodes also play significant roles in regulating soilborne pathogens (bacteria, fungi and plant-parasitic nematodes) [6]. Thus, nematode diversity in soil is a good indicator of soil health [7] and associated with sustainable agriculture [8]. Plant-parasitic nematodes, on the other hand, weaken plants, and reduce the yield and quality of harvests [9].

In order to enhance farmland productivity, fumigants, such as methyl bromide, chloropicrin and 1,3-dichloropropene, and also nematicides including organophosphates and carbamates have been widely used to suppress plant-parasitic nematodes in farmlands [10]. Because of its ozone-depleting property, methyl bromide phased out under the Montreal Protocol [11]. Also, some fumigants and nematicides have been banned or restricted in some countries due to their toxicity to non-target organisms and impact on the environment. For example, a nematicide, carbofuran reduced both total nematode abundance and the number of taxa [12], while another nematicide, aldicarb, also decreased abundances of non-target free-living nematodes [13–15]. Effective chemical nematicides may be potentially harmful to non-target free-living nematodes because of their biocidal activity. Further, imicyafos, another widely used nematicide, did not affect the total numbers of non-target nematodes, but it altered overall nematode fauna evaluated by PCR-DGGE (denaturing gradient gel electrophoresis) [16]. Thus, nematicides with minimum impact on non-target free-living nematodes are desired for promoting farmland productivity by suppressing target plant-parasitic nematodes while keeping free-living nematodes' abundance and diversity.

Environmental conditions after nematicide application, such as temperature, soil moisture and pH, may affect the dissipation of nematicides [17,18]. While rapid dissipation is expected for nematicides, prolonged uses of the same nematicide has been a new problem for controlling plant-parasitic nematodes. This may be due to enhanced biodegradation by soil microbes [19]. Such phenomena have been reported in several nematicides (e.g., aldicarb, cadusafos, oxamyl and fosthiazate) [20–23]. Therefore, a variety of nematicides with different modes of action may be of great demand to avoid potential biodegradation of chemicals due to successive application of a single nematicide [24].

Fluensulfone (5-chloro-2-(3,4,4-trifluorobut-3-enylsulfonyl)-1,3-thiazole; CAS number 318290-98-1) is a heterocyclic fluoroalkenyl sulfone nematicide and its mode of action is different from that of the anticholinesterases and macrocyclic lactones [25]. The target nematodes cover three important plant-parasitic nematode groups, root-knot, root-lesion and cyst nematodes [9]. Efficacies of fluensulfone against the root-knot nematodes *Meloidogyne incognita* and *M. javanica* were shown in different experimental settings, including pot and field experiments using tomato and pepper and in a tomato-cucumber double cropping system, as well as in lima bean fields [26–31]. Fluensulfone was shown to be effective against *Pratylenchus* spp. (root-lesion nematodes) in pot experiments [32], so was against the potato cyst nematode, *Globodera pallida* [33] and sting nematode, *Belonolaimus longicaudatus* [34]. Fluensulfone also showed its efficacy on *Nacobbus aberrans* in pot experiments using tomato and cucumber [35]. Further, fluensulfone has less toxicity to *Caenorhabditis elegans*, a free-living nematode, than to *M. javanica* [25]. Recently, it was reported that fluensulfone had less impact to non-target nematodes in turfgrass, while its damage control of ground cover was limited [36]. For field crops, fluensulfone's efficacy on other free-living nematodes as well as *M. incognita* has not been tested until now.

In this study, we used tomato and sweet potato crops in fields to test the efficacy of fluensulfone on nematodes, since tomato and sweet potato are major hosts of *Meloidogyne* sp. [37,38], which reduced their yields by 20.6% and 10.2%, respectively [9]. In Japan, both tomato and sweet potato are very important agricultural products and their total productions in 2017 were ca 2.2 billion and ca 0.9 billion dollars, respectively [e-Stat: Portal Site of Official Statistics of Japan website (https://www.e-stat.go.jp/)].

Our hypothesis was that fluensulfone may be an efficient means to control root-knot nematodes in tomato and sweet potato. We further hypothesized that fluensulfone might not adversely affect the overall non-target free-living nematode fauna and population density. Therefore, the objectives of the current study were to confirm the efficacy of fluensulfone for root-knot nematodes and to explore the effects of fluensulfone on a broad range of non-target free-living nematodes, which are key players in sustainable crop production [7]. This study will provide in-depth insights into proper use of nematicides for farmers and researchers in the perspective not only from the efficacy on plant-parasitic nematodes but also from the impact on non-target free-living nematodes.

2. Materials and Methods

2.1. Experimental Fields

Four field experiments were conducted in *Meloidogyne* sp. infested fields. In experiments (1) and (2) tomato (*Solanum lycopersicum*) plants were grown in the summer of 2016 and the autumn of 2017 at Japan Plant Protection Association in Ushiku, Japan (35°57′44″ N, 140°10′23″ E), ca 70 km north east of Tokyo (Ushiku I and Ushiku II). In experiment (3), tomato plants were grown in the summer of 2018 at Japan Plant Protection Association in Miyazaki, Japan (32°00′01″ N, 131°27′23″ E), ca 870 km south west of Tokyo (Miyazaki). In experiment (4) sweet potato (*Ipomoea batatas*) plants were grown in the summer of 2018 at Chiba Prefectural Agriculture Research Center (35°32′40″ N, 140°11′29″ E), ca 50 km south east of Tokyo (Chiba). The soils were Ushiku: light clay (sand 40%, silt 26%, clay 33% with 31.6 mg C g^{-1}, 3.1 mg N g^{-1}, pH (H_2O) 6.2 and electric conductivity (EC) of 0.12 mS cm^{-1}), Miyazaki: silty clay loam (sand 17%, silt 45%, clay 38% with 61.0 mg C g^{-1}, 4.2 mg N g^{-1}, pH (H_2O) 4.9 and EC of 0.49 mS cm^{-1}) and Chiba: light clay (sand 35%, silt 40%, clay 25% with 54.4 mg C g^{-1}, 4.6 mg N g^{-1}, pH (H_2O) 5.9 and EC of 0.10 mS cm^{-1}). Trials consisted of (1) a tomato crop planted in June in 2016, (2) a tomato crop planted in September in 2017, (3) a tomato crop planted in May 2018, and (4) a sweet potato crop planted in May 2018. The sizes of an individual plot were (1) and (2) 3.6 m long and 1.8 m wide (6.5 m^2) with 18 tomato plants in two rows (nine plants/row), (3) 5.5 m long and 1.5 m wide (8.3 m^2) with 22 tomato plants in two rows (11 plants/row), and (4) 6 m long and 2 m wide (12 m^2) with 17 potato plants in a row.

2.2. Chemicals

The experimental plots of Ushiku I were treated with two nematicides, fluensulfone (in a granular form, 2% active ingredient; a.i.) supplied by ADAMA JAPAN K.K. (Tokyo, Japan) and fosthiazate (Nemathorin in a granular form, 1.5% a.i., Ishihara Sangyo Kaisha, Tokyo, Japan), and a fumigant (97.5% of 1,3-dichloropropene, DCP: Telone II in a liquid form, Dow AgroSciences, Tokyo, Japan) 2 weeks before crop planting, in triplicate. The experimental plots of Ushiku II, Miyazaki, and Chiba were treated with the two nematicides, fluensulfone and fosthiazate, separately just before crop planting, in triplicates. For each individual experiment, the surface 15 to 20 cm soil was tilled and each chemical was incorporated. Non-treated controls were also prepared in triplicates and each treatment was randomly arranged. Fluensulfone, fosthiazate and DCP were applied at 200 kg ha^{-1} in granular form (4 kg a.i. ha^{-1}), 200 kg ha^{-1} of Nemathorin (3 kg a.i. ha^{-1}), and 150 L ha^{-1} of Telone II (177 kg a.i. ha^{-1}), respectively. The plots applied with DCP after tillage were covered in plastic mulch until planting tomato seedlings.

2.3. Soils and Roots

Soils were collected at 0–15 cm depth, where chemicals were well mixed, at five randomly selected spots in each plot (3 replicates separately) just before chemical applications, 1- and 2-months after planting for all the experiments. The soils were passed through a 5 mm aperture sieve to remove rocks and debris, well mixed and kept at room temperature for no more than 2 days before nematode extraction. At the end of each experiment (2 months after planting for Ushiku I, Ushiku II, and Miyazaki, and 4 months after planting for Chiba), tomato roots and sweet potato tuberous roots were collected, and nematode-induced root galls were counted.

2.4. Nematodes

Nematodes were extracted in triplicate from 20 g subsample of each well mixed soil sample to evaluate nematode fauna using the Baermann funnel extraction method (room temperature, 72 h), and counted under a stereomicroscope (BX53, Olympus, Tokyo, Japan). The soils were confirmed to be infested by *M. incognita* by identifying the extracted root-knot nematodes with PCR-RFLP (restriction fragment length polymorphism) [39]. Occasional occurrences of *Pratylenchus penetrans*, *Paratylenchus* sp., *Trichodorus* sp. and *Xiphinema* sp. were observed, but not considered in this study because of their relatively low populations. Free-living nematodes were counted in total and classified separately for the first 100 individuals or all, if total numbers were less than 100, based on their morphological characters [40] and general feeding habits [41]. The classification of free-living nematodes in the current study covered *Acrobeloides*, *Cephalobus*, *Rhabditis*, other genus in the Rhabditidae family, and the other bacterial feeders. The other feeding types including fungal feeders (*Aphelenchus*, *Aphelenchoides*, *Filenchus* and *Ditylenchus*) and mostly omnivorous nematodes in the Dorylaimida order were also recorded. The proportion of each nematode classification to the total free-living nematodes was shown in the Supplementary Table S1, in which the proportion of *Acrobeloides* and that of frugivorous and omnivorous nematodes, among other nematode groups, showed noticeable fluctuation after chemical treatments. Therefore, we further statistically analyzed the proportion of *Acrobeloides* and that of fungivorous and omnivorous nematodes.

2.5. Galls on Root Systems

Ten out of 18 (Ushiku I and Ushiku II), 22 (Miyazaki) tomato plants, and 17 sweet potato plants (Chiba) in each plot were randomly selected to evaluate root galling. Nematode damage to roots was assessed per plant using a 5-scale index system (0 = no galling, 4 = abundant galling) and was converted into disease index expressed as 0–100 based on the formula: disease index = (the number of infested plants in each index × each index scale)/(4 × total number of plants) [42,43].

2.6. Statistical Analysis

The Shannon-Wiener index (*H*′) was used to evaluate diversity of soil free-living nematode fauna and the Simpson's *D* was applied to assess dominance of abundant taxa [44]. Species richness (Margalef index) and evenness *J*′ was evaluated using genus and family levels as taxa classification [44]. Maturity index [45,46], maturity index (colonizer-persister (*cp*) value 2–5) [47] and maturity index (Cephalobidae adjusted; Cephalobidae's *cp* adjusted from 2 to 1 to reflect the fact that Cephalobidae can be the first colonizer in the experimental fields) were also used to gauge the condition of the soil ecosystem. All the indices were calculated primarily following Yeates and Bongers [7]. Values of each indicator before chemical application were not significantly different ($p > 0.183$) among treatments. At first, the statistical difference of the values in each experiment was analyzed by ANOVA followed by Dunnett's tests, and the analyses were conducted using Microsoft Excel add-in software Statcel (3rd ed.; OMS, Tokyo, Japan). Then, results from the field experiments (combined, excluding the DCP treatment) were also analyzed in R v.3.6.1 [48] using linear mixed-effects models (LMM; lmer library of lme4 package; [49]) for all variables (square-rooted). Chemical treatment was fitted as the categorical explanatory variable and experiment (different soils, hosts and seasons) was treated as a random effect to control for variation in disease index, species abundance, nematode diversity and maturity indices among experiments. To analyze the response of subgroups within nematode fauna a principal component analysis (PCA) was carried out using 9 to 11 nematode species or groups that were present in the samples. PCAs were conducted using Microsoft Excel add-in software Mulcel (OMS, Tokyo, Japan).

3. Results

3.1. Galling on Tomato and Sweet Potato Roots

The disease index in fluensulfone in Ushiku I was just less than 30% (not statistically significant) of that in the non-treated control, and those in Ushiku II, Miyazaki, and Chiba were significantly ($p < 0.01$) lower in fluensulfone treatments than those in the non-treated control (Figure 1). The disease index in DCP (Ushiku I) was significantly ($p < 0.05$) lower than that in the non-treated control, so ($p < 0.01$) was that in a fosthiazate treatment in Chiba (Figure 1). A mixed-effect model among the four experiments showed that the disease index was significantly ($p < 0.001$) lower in fluensulfone treatments than in the non-treated control but that in fosthiazate treatments was not ($p = 0.210$).

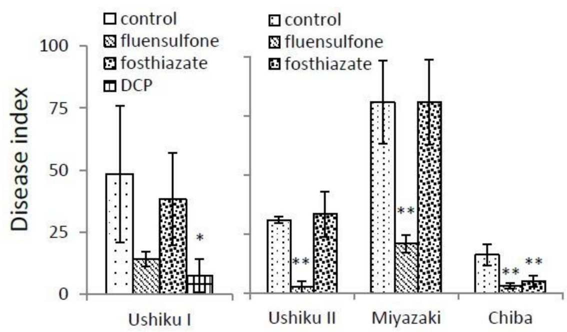

Figure 1. Disease index in Ushiku I, Ushiku II and Miyazaki at 2-months after planting, and Chiba at 4-months after planting. Experimental plots were treated with fluensulfone (4 kg active ingredient (a.i.) ha^{-1}), fosthiazate (3 kg a.i. ha^{-1}), and 1,3-dichloropropene (DCP, 177 kg a.i. ha^{-1}), or non-treated as a control in triplicates. Each value is the mean of three replicates ± standard deviation (** and *: Dunnett's test, $p < 0.01$ and $p < 0.05$, respectively).

3.2. Free-Living Nematode Assemblage

At 1-month after planting, the number of free-living nematodes was significantly ($p < 0.05$) lower in DCP than that in the non-treated control, but not in the other treatments (Figure 2A). At 2-months after planting, the free-living nematode numbers were similar among treatments (Figure 2B). A mixed-effect model at 1- and 2-months among the four experiments did not show significant ($p > 0.082$) difference among treatments.

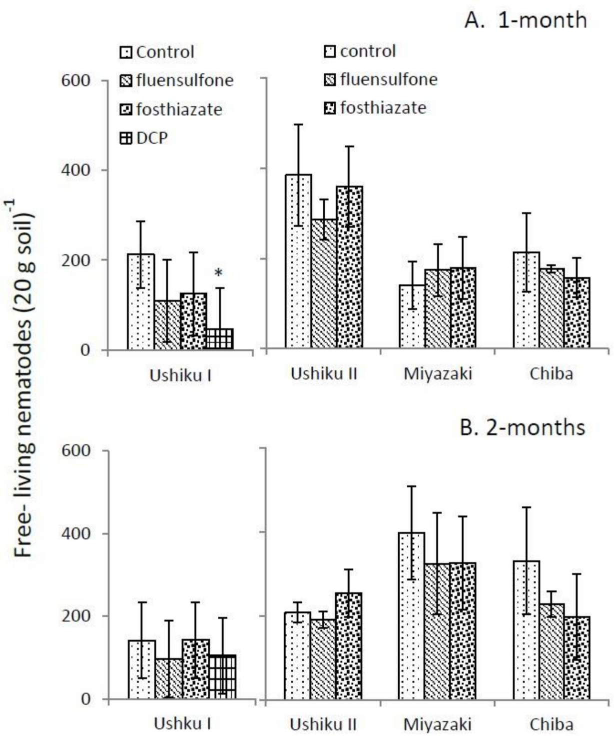

Figure 2. Free-living nematode density (20 g soil)$^{-1}$ in Ushiku I, Ushiku II, Miyazaki and Chiba at (**A**): 1- and (**B**): 2-months after planting. Experimental plots were treated with fluensulfone (4 kg active ingredient (a.i.) ha^{-1}), fosthiazate (3 kg a.i. ha^{-1}), and 1,3-dichloropropene (DCP, 177 kg a.i. ha^{-1}), or non-treated as a control in triplicates. Each value is the mean of three replicates ± standard deviation (*: Dunnett's test, $p < 0.05$).

3.3. Diversity of Free-Living Nematodes

3.3.1. Shannon-Wiener Index (*H′*) and Simpson's *D*

For the entire period (just before chemical applications to 2 months after planting), the values of Shannon-Wiener index (*H′*) in fluensulfone treatments were not significantly different from those in the non-treated control for each individual experiment (Figure 3A,B). The values of *H′* in fosthiazate in Ushiku II and Chiba at 1-month after planting and in Ushiku I at 2-months after planting were significantly ($p < 0.05$) lower than that in the non-treated control, so were the values in DCP at 1- and 2-months after planting. A mixed-effect model among the four experiments at 1- and 2-months after planting showed that the values of *H′* were significantly ($p < 0.001$) lower in fosthiazate treatments than in the non-treated control, but those in fluensulfone were not ($p > 0.447$). The values of Simpson's *D* in Ushiku II and Chiba at 1-month after planting were significantly ($p < 0.05$) higher than those in the non-treated control, so were in DCP at 1- and 2-months after planting (Figure 3C,D). A mixed-effect model among the four experiments at 1- and 2-months after planting showed that *D* was significantly ($p < 0.01$) higher in fosthiazate treatments than in the non-treated control but those in fluensulfone were not ($p > 0.467$).

3.3.2. Species Richness and Evenness *J′*

The values of species richness (Margalef index) in fluensulfone were not different from those in the non-treated control for each individual experiment (Figure 4A,B). Those in fosthiazate in Miyazaki at 1-month after planting and in Ushiku II at 2-months after planting were significantly ($p < 0.01$) lower than that in the non-treated control, so was DCP at 2-months after planting (Figure 4B). A mixed-effect model among the four experiments showed that species richness was significantly ($p < 0.05$) lower in fosthiazate treatment than in the non-treated control at 1- and 2-months after planting. A similar and clearer trend was seen in evenness *J′*. The values in fosthiazate at 2-months after planting and DCP at 1- and 2-months after planting in Ushiku I were significantly ($p < 0.05$) lower than those in the non-treated control (Figure 4C,D). The values of *J′* in fosthiazate treatments in Ushiku II and Chiba at 1-month after planting were also significantly ($p < 0.05$) lower than those in the non-treated control. A mixed-effect model among the four experiments showed that the values of *J′* were significantly ($p < 0.001$) lower in the fosthiazate treatments than in the non-treated control at 1- and 2-months after planting, but those in fluensulfone treatments were not ($p > 0.448$).

3.3.3. Maturity Indices

The values of maturity index were not significantly different among all the treatments in the four experiments (Figure 5A,B). In contrast, the values of maturity index (*cp*2–5) in fosthiazate treatments in Ushiku I at 2-months after planting and Miyazaki at 1- and 2-months after planting were significantly ($p < 0.05$) lower than those in the non-treated control (Figure 5C,D). Those in DCP at 1- and 2-months after planting were significantly ($p < 0.05$) lower than those in the non-treated control. A mixed-effect model among the four experiments showed that maturity index (*cp*2–5) was significantly ($p < 0.05$) lower in a fosthiazate treatment than the non-treated control at 1-month and 2-months after planting, so was that in a fluensulfone treatment but only in 2-months. A mixed-effect model among the four treatments showed that the values of maturity index (Cephalobidae adjusted) in fosthiazate treatments at 1- and 2-months after planting were significantly ($p < 0.01$) lower than in the non-treated control, but those in fluensulfone treatments were not ($p > 0.101$).

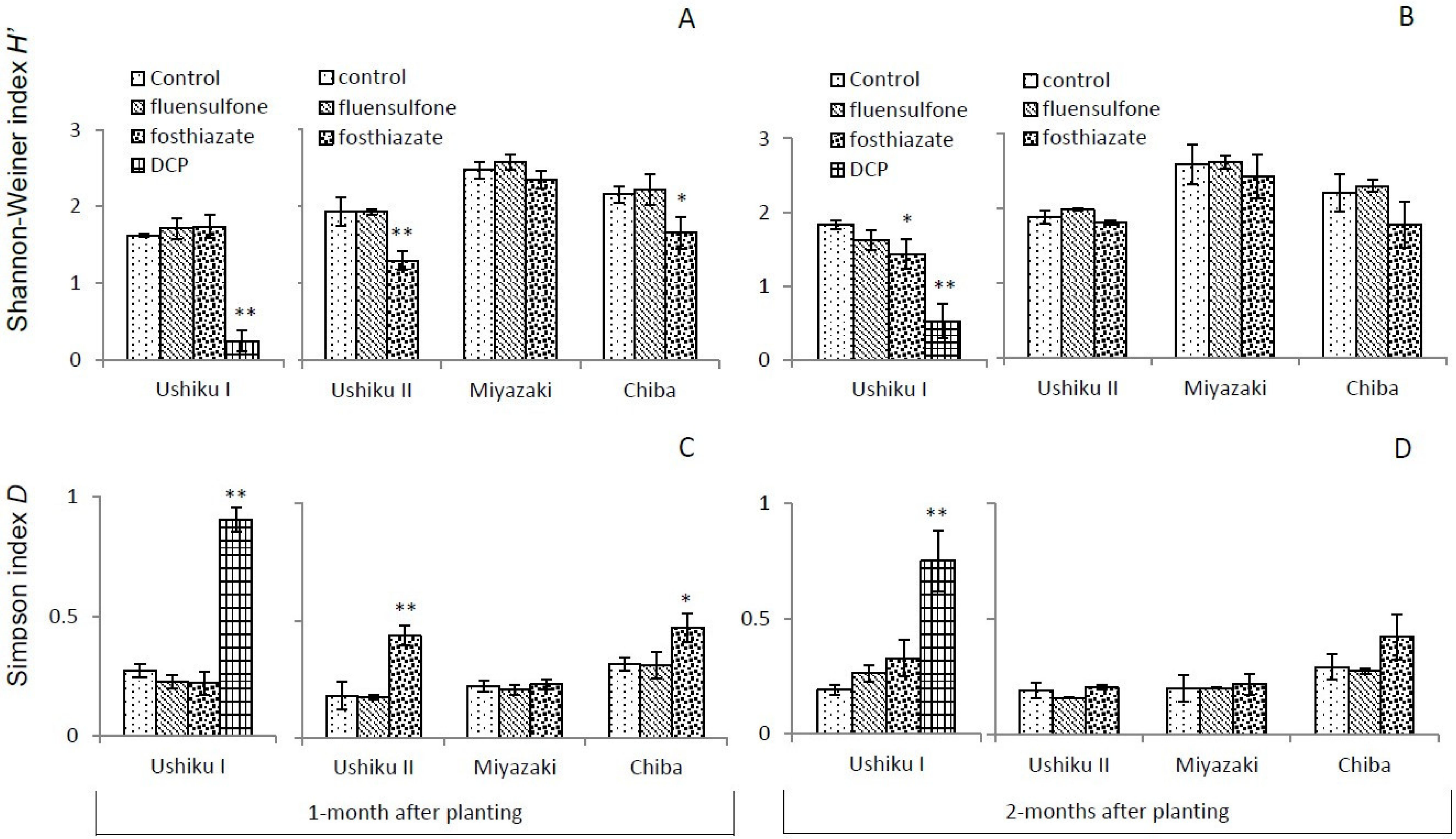

Figure 3. Shannon-Wiener index H' (**A**,**B**) and Simpson index D (**C**,**D**) in Ushiku I, Ushiku II, Miyazaki and Chiba at 1- (**A**,**C**) and 2-months (**B**,**D**) after planting. Experimental plots were treated with fluensulfone (4 kg active ingredient (a.i.) ha^{-1}), fosthiazate (3 kg a.i. ha^{-1}), and 1,3-dichloropropene (DCP, 177 kg a.i. ha^{-1}), or non-treated as a control. Each value is the mean of three replicates ± standard deviation (** and *: Dunnett's test, $p < 0.01$ and $p < 0.05$, respectively).

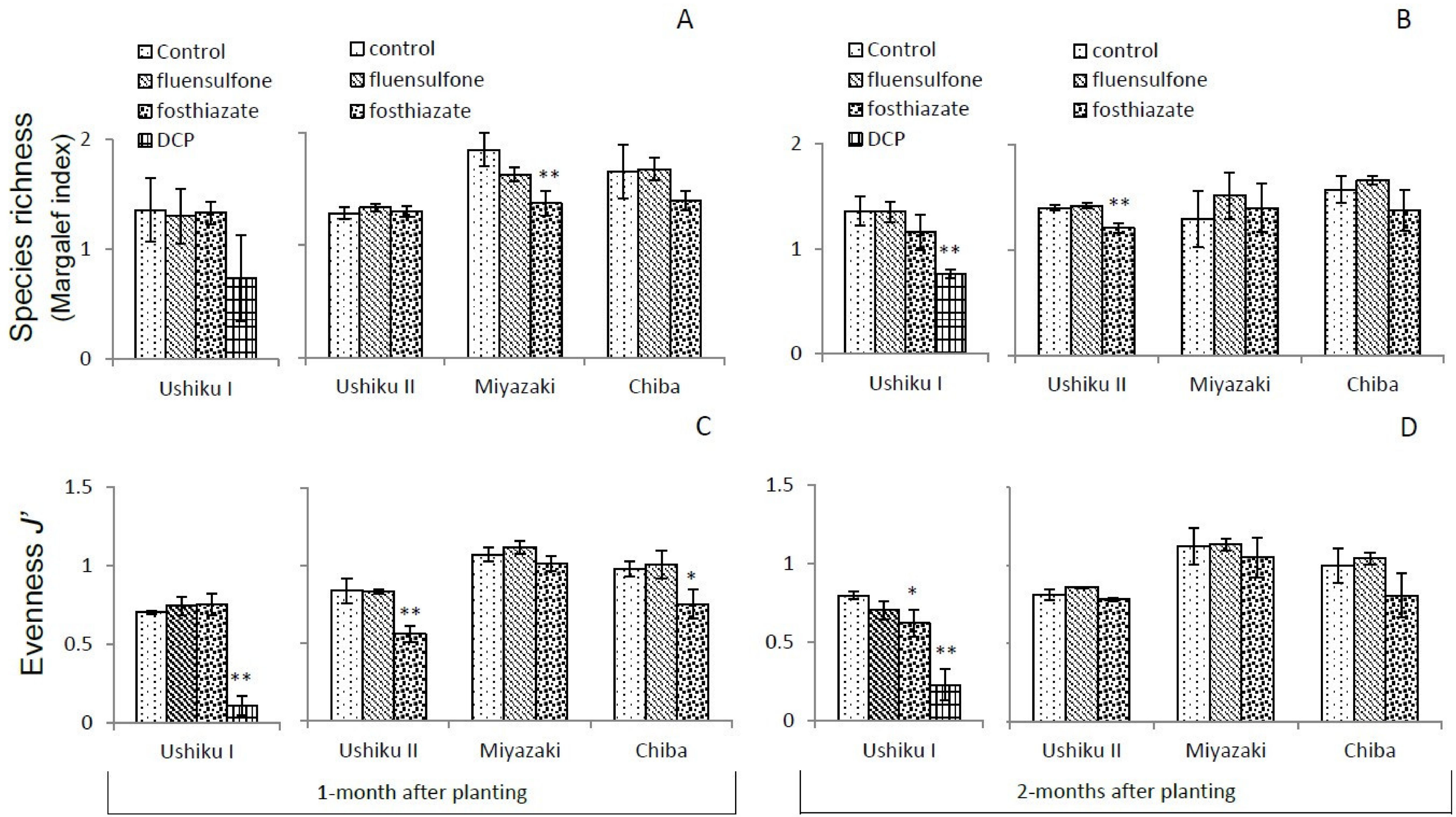

Figure 4. Species richness (Margalef index; (**A**,**B**)) and Evenness *J'* (**C**,**D**) in Ushiku I, Ushiku II, Miyazaki and Chiba at 1- (**A**,**C**) and 2-months (**B**,**D**) after planting. Experimental plots were treated with fluensulfone (4 kg active ingredient (a.i.) ha^{-1}), fosthiazate (3 kg a.i. ha^{-1}), and 1,3-dichloropropene (DCP, 177 kg a.i. ha^{-1}), or non-treated as a control. Each value is the mean of three replicates ± standard deviation (** and *: Dunnett's test, $p < 0.01$ and $p < 0.05$, respectively).

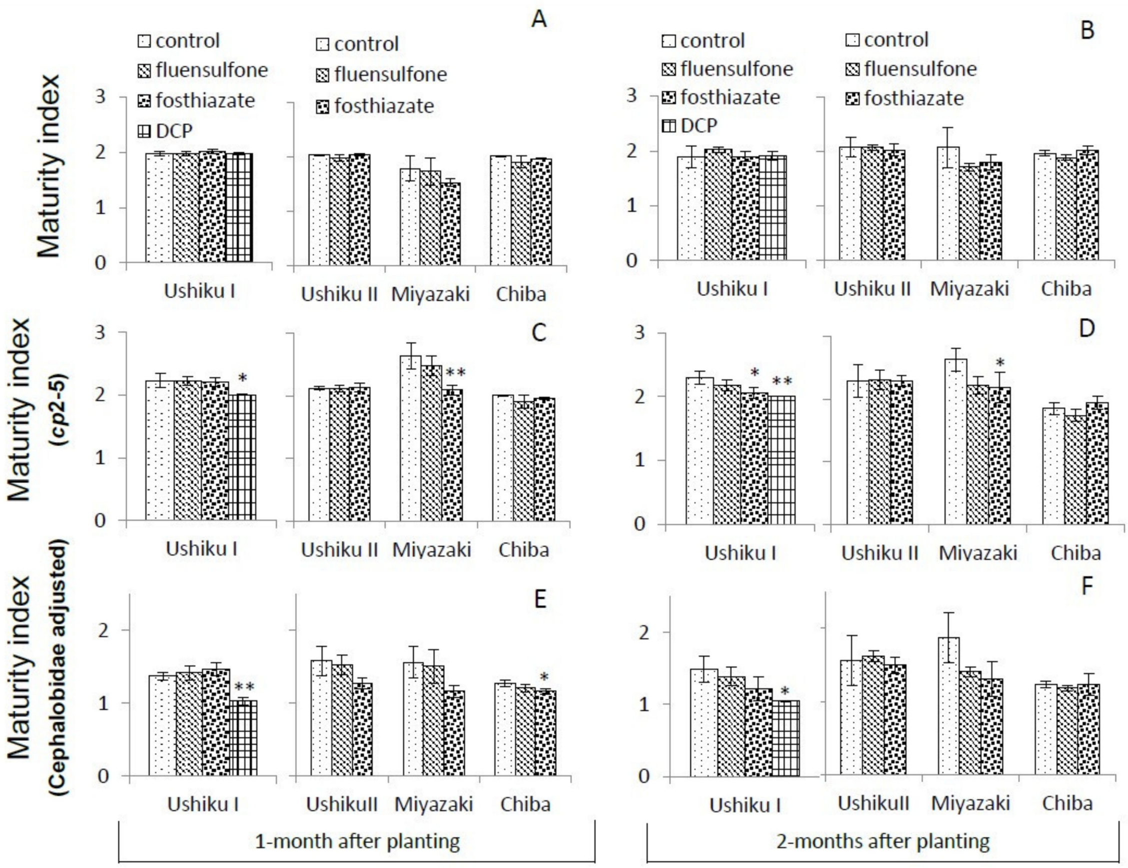

Figure 5. Maturity index (**A**,**B**), Maturity index (*cp*2–5; (**C**,**D**)) and Maturity index (Cephalobidae adjusted; (**E**,**F**)) in Ushiku I, Ushiku II, Miyazaki and Chiba at 1- (**A**,**C**,**E**) and 2-months (**B**,**D**,**F**) after planting. Experimental plots were treated with fluensulfone (4 kg active ingredient (a.i.) ha^{-1}), fosthiazate (3 kg a.i. ha^{-1}), and 1,3-dichloropropene (DCP, 177 kg a.i. ha^{-1}), or non-treated as a control. Each value is the mean of three replicates ± standard deviation (** and *: Dunnett's test, $p < 0.01$ and $p < 0.05$, respectively).

3.3.4. *Acrobeloides* sp., and Fungivorous and Omnivorous Nematodes

For each individual experiment, the proportions of *Acrobeloides* sp. to the total free-living nematodes in fluensulfone were not different from those in the non-treated control (Figure 6A,B). Those in fosthiazate were significantly ($p < 0.05$) higher in Ushiku II, Miyazaki and Chiba at 1-month after planting and in Ushiku I, Miyazaki and Chiba at 2-months after planting. Those in DCP were significantly ($p < 0.01$) higher than those in the non-treated control at 1- and 2-months after planting (Figure 6A,B). A mixed-effect model among the four experiments showed that fosthiazate treatments at 1- and 2-months after planting were significantly ($p < 0.001$) higher in the value than the non-treated control, so was fluensulfone treatment at 2-months ($p < 0.05$) but not at 1-month ($p = 0.958$). Fungivorous and omnivorous nematodes' proportions to the total free-living nematodes in fluensulfone and the non-treated control were not statistically different in each individual experiment (Figure 6C,D). The proportions in DCP at 1- and 2-months after planting were significantly ($p < 0.01$) lower than those of the non-treated control. A mixed-effect model among the four experiments showed that fosthiazate treatments at 1- and 2-months after planting were significantly ($p < 0.001$) lower in the value than the non-treated control, but fluensulfone treatments were not ($p > 0.427$).

3.3.5. Principal Component Analysis

The result of PCA analysis showed that DCP in Ushiku I, and fosthiazate in Ushiku II and Chiba after chemical treatments were seen in the dotted circles (Figure 7), which were remote from the other treatments. Among the loading factors (LF) for Ushiku I, Ushiku II and Chiba, the values of *Acrobeloides* sp. were over 0.98, while most of the other LF values were negative. *Rhabditis* sp. was the most important LF value (0.99) for Miyazaki (Table 1).

Table 1. Principal component analysis.

	Ushiku I		Ushiku II		Miyazaki		Chiba	
	Principal Components		Principal Components		Principal Components		Principal Components	
	1st	2nd	1st	2nd	1st	2nd	1st	2nd
Component ratio	0.81	0.09	0.69	0.16	0.52	0.20	0.52	0.34
Cumulative component ratio	0.81	0.91	0.69	0.86	0.52	0.72	0.52	0.86
Loading factor								
Acrobeloides sp.	1.00	0.03	1.00	0.05	−0.50	−0.41	0.98	0.17
Other Cephalobidae	−0.64	0.76	−0.44	0.19	−0.68	0.06	−0.45	0.89
Rhabditis sp.	−0.74	−0.42	−0.28	−0.84	0.99	0.04	−0.39	−0.77
Other Rhabditidae	−0.61	−0.24	−0.27	−0.54	0.00	−0.80	−0.29	−0.30
Other bacterivore	−0.59	−0.41	−0.67	−0.51	−0.47	0.18	−0.28	−0.63
Aphelenchus sp.	−0.45	−0.07	−0.37	0.57	0.43	−0.31	−0.41	−0.57
Aphelenchoides sp.	−0.09	−0.27	−0.60	0.70	0.31	0.06	−0.20	−0.41
Filenchus sp.	−0.30	−0.08	−0.53	0.52	−0.53	0.39	−0.32	0.01
Ditylenchus sp.	−0.08	−0.11	0.23	0.16	−0.40	0.22	-	-
Dorylaimida	−0.61	−0.25	−0.34	−0.82	−0.20	0.81	−0.31	−0.26
Other	-	-	-	-	0.36	−0.13	-	-

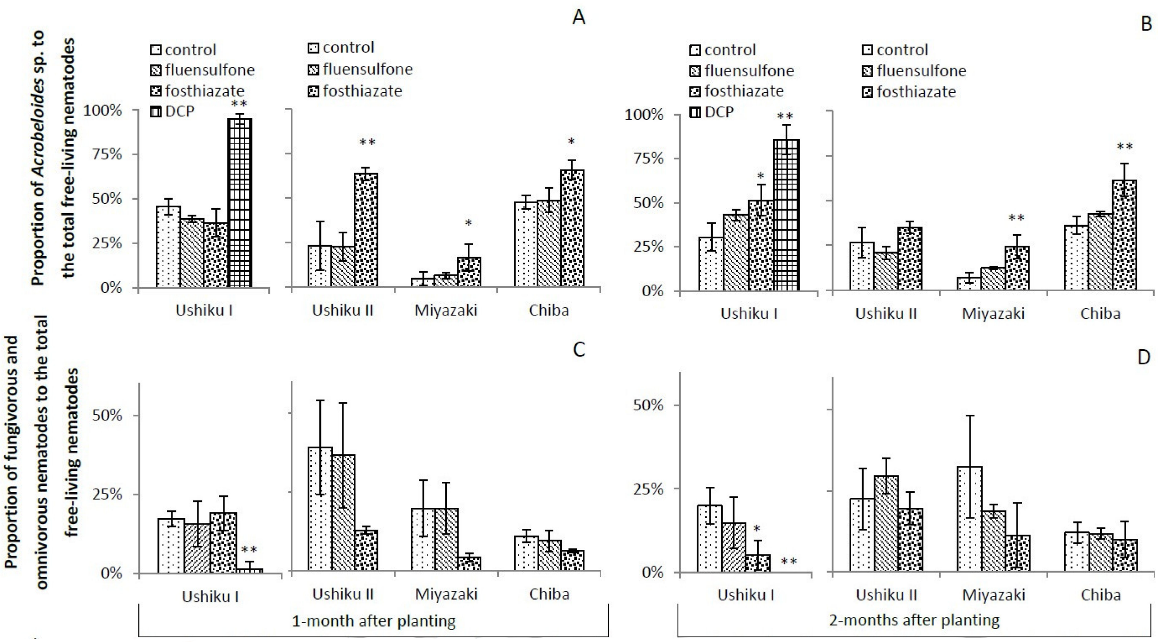

Figure 6. Proportion of *Acrobeloides* sp. (**A**,**B**) and that of fungivorous and omnivorous nematodes (**C**,**D**) to the total free-living nematodes in Ushiku I, Ushiku II, Miyazaki and Chiba at 1- (A,**C**) and 2-months (**B**,**D**) after planting. Experimental plots were treated with fluensulfone (4 kg active ingredient (a.i.) ha^{-1}), fosthiazate (3 kg a.i. ha^{-1}), and 1,3-dichloropropene (DCP, 177 kg a.i. ha^{-1}), or non-treated as a control. Each value is the mean of three replicates ± standard deviation (** and *: Dunnett's test, $p < 0.01$ and $p < 0.05$, respectively).

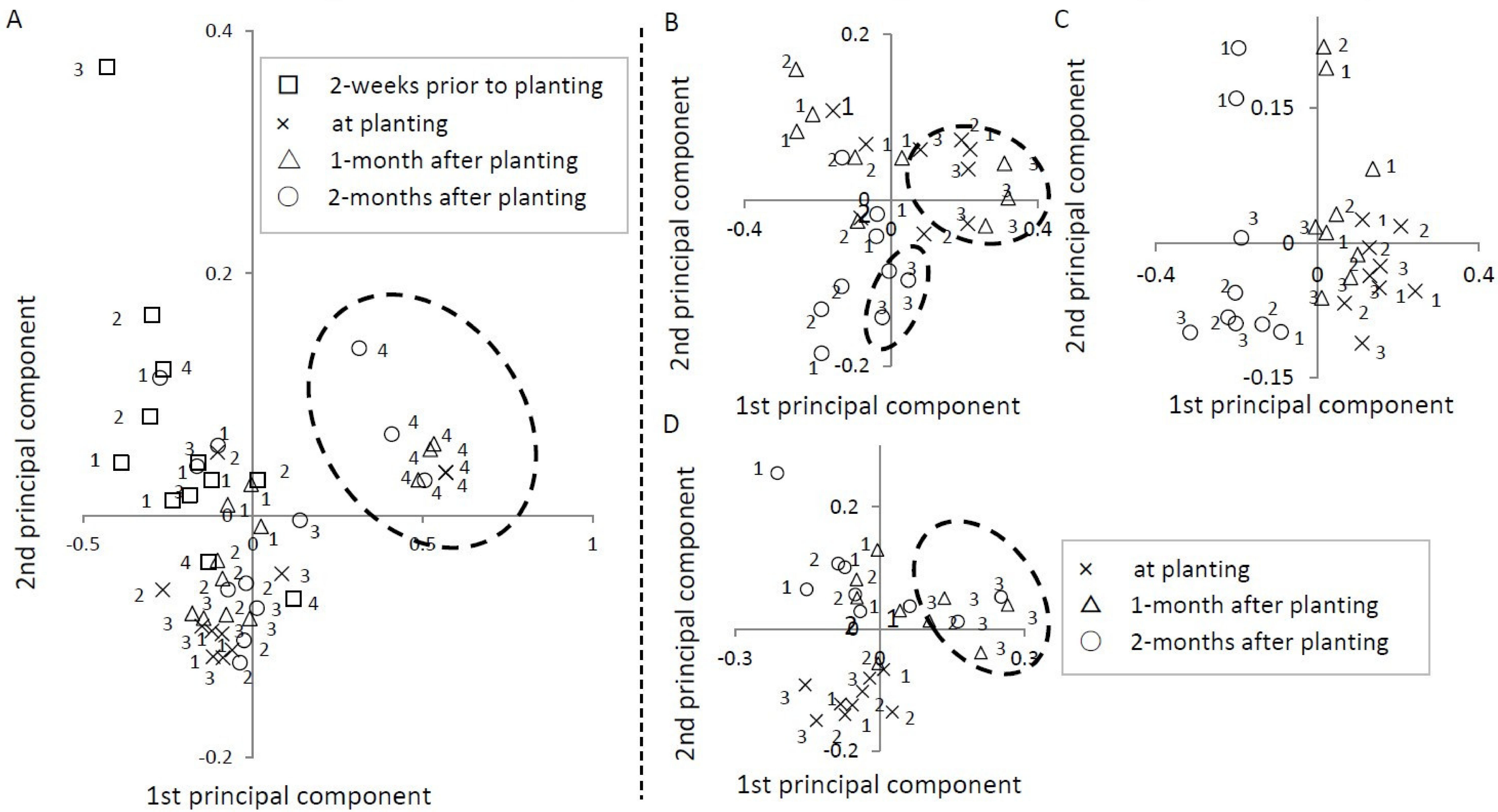

Figure 7. Principal component analysis for (**A**): Ushiku I, (**B**): Ushiku II, (**C**): Miyazaki and (**D**): Chiba. Experimental plots were treated with fluensulfone (4 kg active ingredient (a.i.) ha^{-1}), fosthiazate (3 kg a.i. ha^{-1}) and 1,3-dichloropropene (DCP, 177 kg a.i. ha^{-1}), or non-treated as a control in triplicates. Numbers in the graphs indicate 1: non-treated control, 2: fluensulfone, 3: fosthiazate and 4: DCP.

4. Discussion

The disease index analysis results confirmed the effectiveness of fluensulfone against root-knot nematodes [26–31], though the main focus of this study was to evaluate fluensulfone's nematicidal activity against non-target free-living nematodes. The present study revealed that fluensulfone is a nematicide with little impact on non-target free-living nematodes. The fluensulfone treatment did not affect the total number of free-living nematodes throughout the experimental period in each individual experiment conducted in three locations and in different hosts and seasons. The nematode diversity level in the fluensulfone treatment, shown by Shannon-Wiener index (*H′*), an important indicator of biodiversity in soil [7], was also consistently similar to that in the non-treated control. As indicated by Simpson's *D*, which generally amplifies the impact of high density species [50], nematode diversity in a fluensulfone treatment did not heavily rely on high density species. The results observed in *H′* and *D* were supported by species richness (Margalef index), evenness *J′* and maturity indices as they were the same levels between the fluensulfone treatment and the non-treated control. Further, the proportion of *Acrobeloides* sp. and that of fungivorous and omnivorous nematodes to the total free-living nematodes were consistently at very similar levels in both the fluensulfone treatment and the non-treated control for each individual experiment over the experimental periods. This was supported by PCA analysis, which also showed consistently similar results of fluensulfone treatments to those of the non-treated control. These results concluded that fluensulfone has very little effect on the free-living nematode fauna in soil. As previous studies reported [4,5], diverse free-living nematodes play important roles in soil ecosystem function, such as nutrient cycling, decomposition and disease suppression [2]. Fluensulfone may serve well for maintaining a diverse free-living nematode community while suppressing root-knot nematodes.

Fosthiazate treatments, except in Chiba, were not effective against root-knot nematodes, unlike previous studies [51–53], yet, the exact reason for this is uncertain. Fosthiazate treatments did not affect the total free-living nematodes density for each individual experiment, and the result of this non-response is consistent with findings of a previous study [54]. Diversity of free-living nematodes, however, was affected by fosthiazate treatments, as presented in *H′*, *D*, species richness, *J′*, maturity index (Cephalobidae adjusted), all of which indicated significantly different results of fosthiazate treatments from the non-treated control. PCA also implied that fosthiazate affected the free-living nematode fauna. As indicated in the proportions of *Acrobeloides* sp., and fungivorous and omnivorous nematodes to the total free-living nematodes, fosthiazate did not reduce the population of *Acrobeloides*, but reduced the populations of fungivorous and omnivorous nematodes. On this point, Sturz and Kimpinski [55] showed that fosthiazate did not affect bacterivorous nematodes, to which *Acrobeloides* belongs.

DCP expelled most of nematodes in the soils, including both root-knot and free-living nematodes. Since DCP treatment killed the nematodes almost completely, nematode diversity was lost. Even at 2-months after planting, the level of diversity was very low and heavily relied on limited species as indicated by *H′*, *D*, species richness, *J′*, and maturity indices (*cp*2–5 and Cephalobidae adjusted). The overall results were consistent with previous studies [56–61]. The species recovered first in the DCP treatment was *Acrobeloides* sp., while fungivorous and omnivorous nematodes did not recover until the end of the experiment. The results are consistent with those of Okada et al. [62] who showed that Cephalobidae nematodes, to which *Acrobeloides* sp. belongs, increased greatly in the first 2 months after fumigation. Though this study did not cover the long-term effect, Sánchez-Moreno et al. [59] and Timper et al. [60] reported recovery of omnivorous nematodes in 22 weeks (by treating DCP plus chloropicrin) and by the following season (by treating DCP plus aldicarb), respectively.

Maturity index in each chemical treatment was not different from that in the non-treated control. This may be due to the simple colonizer-persister (*cp*) value appointment for each nematode species. Except Miyazaki, 75% or more of the free-living nematodes in each experimental location was in the category of *cp*2 on average. Also, especially in the non-treated control, Dorylaimida with a high *cp* value (*cp*4) and Rhabditidae with a low *cp* value (*cp*1), may be offset. Dorylaimida and Rhabditidae at

2-months after planting in DCP were 0% and very limited (< 2%), respectively. As a result of offsetting high and low *cp* value nematode classifications, the end maturity index levels converged to ca 2 due to relatively abundant Cephalobidae (*cp*2) including *Acrobeloides* sp. Since the proportion of *cp*1 and *cp*4 nematodes in Miyazaki were relatively higher than the other experimental locations, maturity index (*cp*2–5) may be more sensible than maturity index for the difference among the treatments. On this point, Yeates [63] indicated that the dominant nematode species may be different depending on resource and soil texture. Okada et al. [62] further discussed that depending on soil types Cephalobidae may be the first colonizer and increase rapidly. Using another maturity index (*cp*2–5) which excludes enrichment opportunists (*cp*1), the consistent conditions of the soil nematode fauna with the other indices of ecological status were observed to a certain extent. Further, since Cephalobidae may play as the first colonizer in the fields of this study, maturity index (Cephalobidae adjusted) was tested by reassigning the *cp* value of Cephalobidae from 2 to 1 as an alternative indicator in this particular environment. Though maturity index (Cephalobidae adjusted) may be more capable to highlight the difference among treatments than the other maturity indices in this study, further analysis in a variety of field environments may be desired. As Okada et al. [62] indicated, due care for using maturity indices may be essential especially in case of the presence of dominant Cephalobidae, yet maturity index (*cp*2–5) and even maturity index (Cephalobidae adjusted) may be useful in evaluating the condition of free-living nematode fauna.

PCA reinforced the discussion made on the several different indices by highlighting a certain nematode classification as an important factor in the four experiments. Depending on the experimental locations, there were certain differences in the importance of the 1st and 2nd component ratios and the loading factors (LF). *Acrobeloides* sp. was the most important LF (more than 0.75) except Miyazaki, where *Acrobeloides* sp. was still one of the important LF (−0.50; the most important LF in Miyazaki was *Rhabditis* sp.: 0.99). This is consistent with the discussion for the proportion of *Acrobeloides* sp. to the total free-living nematodes. In all the experiments, PCA showed that fluensulfone treatments were not different from the non-treated control, while fosthiazate in Ushiku II and Chiba and DCP treatments were in different positions. DCP demonstrated an obvious difference shown in the remote plots in the PCA graphs. In Ushiku II and Chiba, PCA also revealed that fosthiazate treatments were in separate areas from the non-treated control and fluensulfone treatments to some extent.

The current study used nine to 11 different nematode classifications to measure nematode diversity, though Stirling and Wilsey [64] discussed richness of > 10 and < 100 species fits for modeling biodiversity using H'. There were possibly more species existed in the tested fields, however, using this level of classification may be an empirically feasible approach for field studies considering the robust process for nematode identification and quantification. Also, the present study applied several different measurements including H', D, J', maturity indices and PCA to figure out the status of nematode diversity in each experiment. As Bardgett and van der Putten [65] mentioned, belowground communities are remarkably diverse and the theoretical models to explain patterns of belowground community organization are still under development.

5. Conclusions

As a conclusion, fluensulfone was an effective nematicide against galling on tomato and sweet potato roots by root-knot nematodes with very limited impact on the soil free-living nematode fauna. This is the first report of fluensulfone's nematicidal activity against *M. incognita*, but less activity against non-target free-living nematode fauna in field crops.

Supplementary Materials: For the details of each experiment, the following is available online at http://www.mdpi.com/2073-4395/9/12/853/s1, Table S1: Proportion of each nematode classification to the total free-living nematodes.

Author Contributions: Conceptualization, M.K. and K.T.; Methodology, M.K., K.T. and D.H.; Investigation, M.K. and T.F.; Data curation, M.K.; Formal analysis, M.K.; Writing—Original draft preparation, M.K.; Writing—Review and editing, M.K., K.T., T.F. and D.H.

Funding: This research received no external funding.

Acknowledgments: We acknowledge that Japan Plant Protection Association and Chiba Prefectural Agriculture and Forestry Research Center supported this work, especially for day-to-day management to grow tomato and sweet potato plants, and provided useful information.

Conflicts of Interest: The authors declare no conflict of interest.

References

1. Kennedy, A.C.; Smith, K.L. Soil microbial diversity and the sustainability of agricultural soils. *Plant Soil* **1995**, *170*, 75–86. [CrossRef]
2. Neher, D.A. Ecology of plant and free-living nematodes in natural and agricultural soil. *Annu. Rev. Phytopathol.* **2010**, *48*, 371–394. [CrossRef] [PubMed]
3. Bardgett, R.D.; Cook, R.; Yeates, G.W.; Denton, C.S. The influence of nematodes on below-ground processes in grassland ecosystems. *Plant Soil* **1999**, *212*, 23–33. [CrossRef]
4. Ingham, R.E.; Trofymow, J.A.; Ingham, E.R.; Coleman, D.C. Interactions of bacteria, fungi, and their nematode grazers: Effects on nutrient cycling and plant growth. *Ecol. Monogr.* **1985**, *55*, 119–140. [CrossRef]
5. De Ruiter, P.C.; Moore, J.C.; Zwart, K.B.; Bouwman, L.A.; Hassink, J.; Bloem, J.; De Vos, J.A.; Marinissen, J.C.Y.; Didden, W.A.M.; Lebrink, G.; et al. Simulation of nitrogen mineralization in the below-ground food webs of two winter wheat fields. *J. Appl. Ecol.* **1993**, *30*, 95–106. [CrossRef]
6. Yeates, G.W.; Wardle, D.A. Nematodes as predators and prey: Relationships to biological control and soil processes. *Pedobiologia* **1996**, *40*, 43–50.
7. Yeates, G.W.; Bongers, T. Nematode diversity in agroecosystems. *Agric. Ecosyst. Environ.* **1999**, *74*, 113–135. [CrossRef]
8. Mulder, C.; Zwart, D.; Van Wijnen, H.J.; Schouten, A.J.; Breure, A.M. Observational and simulated evidence of ecological shifts within the soil nematode community of agroecosystems under conventional and organic farming. *Funct. Ecol.* **2003**, *17*, 516–525. [CrossRef]
9. Sasser, J.N.; Freckman, D.W. A world perspective on nematology: The role of the society. In *Vistas on Nematology*; Veech, J.A., Dickson, D.W., Eds.; Society of Nematologists: Hyattsville, MD, USA, 1987; pp. 7–14.
10. Ciancio, A.; Colagiero, M.; Pentimone, I.; Rosso, L.C. Formulation of *Pochonia chlamydosporia* for plant and nematode management. In *Bioformulations: For Sustainable Agriculture*; Arora, N.K., Mehnaz, S., Balestrini, R., Eds.; Springer: Berlin, Germany, 2016; pp. 177–197. [CrossRef]
11. Protocol, Montreal. *Montreal Protocol on Substances that Deplete the Ozone Layer*; US Government Printing Office: Washington, DC, USA, 1987; Volume 26, pp. 128–136.
12. Chelinho, S.; Sautter, K.D.; Cachada, A.; Abrantes, I.; Brown, G.; Duarte, A.C.; Sousa, J.P. Carbofuran effects in soil nematode communities: Using trait and taxonomic based approaches. *Ecotox. Environ. Safety* **2011**, *74*, 2002–2012. [CrossRef]
13. Wada, S.; Toyota, K.; Takada, A. Effects of the nematicide imicyafos on soil nematode community structure and damage to radish caused by Pratylenchus penetrans. *J. Nematol.* **2011**, *43*, 1–6.
14. Smolik, J.D. Effect of nematicide treatments on nontarget nematode populations associated with corn. *Plant Dis.* **1983**, *67*, 28–31. [CrossRef]
15. Grabau, Z.J.; Chen, S. Influence of long-term corn-soybean crop sequences on soil ecology as indicated by the nematode community. *Appl. Soil Ecol.* **2016**, *100*, 172–185. [CrossRef]
16. Grabau, Z.J.; Vetsch, J.A.; Chen, S. Swine manure, nematicides, and long-term tillage change soil ecology in corn and soybean production. *Agron. J.* **2018**, *110*, 2288–2301. [CrossRef]
17. Mueller, J.D.; Noling, J.W. Standardization of reporting procedures for nematicide efficacy testing: A research and extension perspective. *Supp. J. Nematol.* **1996**, *28*, 575–585.
18. Cáceres, T.; Megharaj, M.; Naidu, R. Degradation of fenamiphos in soils collected from different geographical regions: The influence of soil properties and climatic conditions. *J. Environ. Sci. Health B* **2008**, *43*, 314–322.
19. Pattison, A.B.; Stanton, J.M.; Cobon, J.A. Bioassay for enhanced biodegradation of nematicides in soil. *Australas. Plant Path.* **2000**, *29*, 52–58. [CrossRef]
20. Read, D.C. Greatly accelerated microbial degradation of aldicarb in re-treated field soil, in flooded soil and in water. *J. Econ. Entomol.* **1987**, *80*, 156–163. [CrossRef]

21. Karpouzas, D.G.; Karanasios, E.; Menkissoglu-Spiroudi, U. Enhanced microbial degradation of cadusafos in soils from potato monoculture: Demonstration and characterization. *Chemosphere* **2004**, *56*, 549–559. [CrossRef]
22. Osborn, R.K.; Haydock, P.P.J.; Edwards, S.G. Isolation and identification of oxamyl-degrading bacteria from UK agricultural soils. *Soil Biol. Biochem.* **2010**, *42*, 998–1000. [CrossRef]
23. Papadopoulou, E.S.; Lagos, S.; Spentza, F.; Vidiadakis, E.; Karas, P.A.; Klitsinaris, T.; Karpouzas, D.G. The dissipation of fipronil, chlorpyrifos, fosthiazate and ethoprophos in soils from potato monoculture areas: First evidence for the enhanced biodegradation of fosthiazate. *Pest Manag. Sci.* **2015**, *72*, 1040–1050. [CrossRef]
24. Noling, J.; Becker, J.O. The challenge of research and extension to define and implement alternatives to methyl bromide. *J. Nematol.* **1994**, *26*, 573–586.
25. Kearn, J.; Ludlow, E.; Dillon, J.; O'Connor, V.; Holden-Dye, L. Fluensulfone is a nematicide with a mode of action distinct from anticholinesterases and macrocyclic lactones. *Pestic. Biochem. Phys.* **2014**, *109*, 44–57. [CrossRef] [PubMed]
26. Oka, Y.; Shuker, S.; Tkachi, N. Nematicidal efficacy of MCW-2, a new nematicide of the fluoroalkenyl group, against the root-knot nematode Meloidogyne javanica. *Pest Manag. Sci.* **2009**, *65*, 1082–1089. [CrossRef] [PubMed]
27. Oka, Y.; Shuker, S.; Tkachi, N. Systemic nematicidal activity of fluensulfone against the root-knot nematode Meloidogyne incognita on pepper. *Pest Manag. Sci.* **2011**, *68*, 268–275. [CrossRef]
28. Oka, Y.; Shuker, S.; Tkachi, N. Influence of soil environments on nematicidal activity of fluensulfone against Meloidogyne javanica. *Pest Manag. Sci.* **2013**, *69*, 1225–1234. [CrossRef]
29. Morris, K.A.; Langston, D.B.; Dickson, D.W.; Davis, R.F.; Timper, P.; Noe, J.P. Efficacy of fluensulfone in a tomato–cucumber double cropping system. *J. Nematol.* **2015**, *47*, 310–315.
30. Castillo, G.X.; Ozores-Hampton, M.; Gine, P.A.N. Effects of fluensulfone combined with soil fumigation on root-knot nematodes and fruit yield of drip-irrigated fresh-market tomatoes. *Crop Prot.* **2017**, *98*, 166–171. [CrossRef]
31. Jones, J.G.; Kleczewski, N.M.; Desaeger, J.; Meyer, S.L.F.; Johnson, G.C. Evaluation of nematicides for southern root-knot nematode management in lima bean. *Crop Prot.* **2017**, *96*, 151–157. [CrossRef]
32. Oka, Y. Nematicidal activity of fluensulfone against some migratory nematodes under laboratory conditions. *Pest Manag. Sci.* **2014**, *70*, 1850–1858. [CrossRef]
33. Norshie, P.M.; Grove, I.G.; Back, M.A. Field evaluation of the nematicide fluensulfone for control of the potato cyst nematode *Globodera pallida*. *Pest Manag. Sci.* **2016**, *72*, 2001–2007. [CrossRef]
34. Grabau, Z.J.; Noling, J.W.; Gine, P.A.N. Fluensulfone and 1,3-dichloropropene for plant-parasitic nematode management in potato production. *J. Nematol.* **2019**, *51*, 1–12. [CrossRef]
35. Cabrera-Hidalgo, A.; Valadez, M.; Marbán, M. Effect of fluensulfone on the mobility in vitro, and reproduction and root galling of Nacobbus aberrans in microplots. *Nematropica* **2015**, *45*, 59–71.
36. Waldo, B.D.; Grabau, Z.J.; Mengistu, T.M.; Crow, W.T. Nematicide effects on non-target nematodes in bermudagrass. *J. Nematol.* **2019**, *51*, 1–12. [CrossRef] [PubMed]
37. Overstreet, C. Nematodes. In *The Sweetpotato*; Loebenstein, G., Thottappilly, G., Eds.; Springer: Berlin, Germany, 2009; pp. 135–159. [CrossRef]
38. Seid, A.; Fininsa, C.; Mekete, T.; Decraemer, W.; Wesemael, W.M. Tomato (*Solanum lycopersicum*) and root-knot nematodes (Meloidogyne spp.)—A century-old battle. *Nematology* **2015**, *17*, 995–1009. [CrossRef]
39. Neher, D.A. Role of nematodes in soil health and their use as indicators. *J. Nematol.* **2001**, *33*, 161–168.
40. Neher, D.A.; Peck, S.L.; Rawlings, J.; Campbell, C.L. Measures of nematode community structure and sources of variability among and within agricultural fields. *Plant Soil* **1995**, *170*, 167–181. [CrossRef]
41. Powers, T.O.; Harris, T.S. A polymerase chain reaction method for identification of five major Meloidogyne species. *J. Nematol.* **1993**, *25*, 1–6.
42. Shishida, Y. Nematoda. In *Pictorial Keys to Soil Animal of Japan*; Aoki, J., Ed.; Tokai University Press: Tokyo, Japan, 1999; pp. 15–38.
43. Yeates, G.W.; Bongers, T.D.; De Goede, R.G.M.; Freckman, D.W.; Georgieva, S.S. Feeding habits in soil nematode families and genera—An outline for soil ecologists. *J. Nematol.* **1993**, *25*, 315–331.
44. Smith, A.L.; Taylor, A.L. Field methods of testing for root-knot infestation. *Phytopathology* **1947**, *37*, 85–93.

45. Ito, K. Evaluation of nematode's damage. In *Nematology Experimental Methods*; The Japanese Nematological Society: Tsukuba, Japan, 2004; pp. 103–105.
46. Bongers, T. The maturity index: An ecological measure of environmental disturbance based on nematode species composition. *Oecologia* **1990**, *83*, 14–19. [CrossRef]
47. Bongers, T.; Korthals, G. The Maturity Index, an Instrument to Monitor Changes in the Nematode Community Structure. In *Proceedings of the 45th International Symposium on Crop Protection Ghent, Belgium*; Wageningen University & Research: Droevendaalsesteeg, The Netherlands, 1993; p. 80.
48. R Core Team. *R: A Language and Environment for Statistical Computing*; R Foundation for Statistical Computing: Vienna, Austria, 2019; Available online: https://www.R.-project.org/ (accessed on 30 July 2019).
49. Bates, D.; Maechler, M.; Bolker, B.; Walker, S. Fitting linear mixed-effects models using lme4. *J. Stat. Softw.* **2015**, *67*, 1–48. [CrossRef]
50. Magurran, A.E. Diversity indices and species abundance models. In *Ecological Diversity and Its Measurement*; Springer: Berlin, Germany, 1988; pp. 7–45. [CrossRef]
51. Pullen, M.P.; Fortnum, B.A. Fosthiazate controls Meloidogyne arenaria and M. incognita in flue-cured tobacco. *J. Nematol.* **1999**, *31*, 694–699. [PubMed]
52. Ingham, R.E.; Hamm, P.B.; Williams, R.E.; Swanson, W.H. Control of Meloidogyne chitwoodi in potato with fumigant and nonfumigant nematicides. *J. Nematol.* **2000**, *32*, 556–565. [PubMed]
53. Radwan, M.A.; Farrag, S.A.A.; Abu-Elamayem, M.M.; Ahmed, N.S. Efficacy of some granular nematicides against root-knot nematode, Meloidogyne incognita associated with tomato. *Pakistan J. Nematol.* **2012**, *30*, 41–47.
54. Wada, S.; Toyota, K. Effect of three organophosphorous nematicides on non-target nematodes and soil microbial community. *Microbes Environ.* **2008**, *23*, 331–336. [CrossRef] [PubMed]
55. Sturz, A.V.; Kimpinski, J. Effects of fosthiazate and aldicarb on populations of plant-growth-promoting bacteria, root-lesion nematodes and bacteria-feeding nematodes in the root zone of potatoes. *Plant Pathol.* **1999**, *48*, 26–32. [CrossRef]
56. Ettema, C.H.; Bongers, T. Characterization of nematode colonization and succession in disturbed soil using the maturity index. *Biol. Fert. Soils* **1993**, *16*, 79–85. [CrossRef]
57. Yeates, G.W.; van der Meulen, H. Recolonization of methyl-bromide sterilized soils by plant and soil nematodes over 52 months. *Biol. Fert. Soils* **1996**, *21*, 1–6. [CrossRef]
58. Sánchez-Moreno, S.; Jiménez, L.; Alonso-Prados, J.L.; García-Baudin, J.M. Nematodes as indicators of fumigant effects on soil food webs in strawberry crops in southern Spain. *Ecol. Indic.* **2010**, *10*, 148–156. [CrossRef]
59. Timper, P.; Davis, R.; Jagdale, G.; Herbert, J. Resiliency of a nematode community and suppressive service to tillage and nematicide application. *Appl. Soil Ecol.* **2012**, *59*, 48–59. [CrossRef]
60. Watson, T.T.; Desaeger, J.A. Evaluation of non-fumigant chemical and biological nematicides for strawberry production in Florida. *Crop Prot.* **2019**, *117*, 100–107. [CrossRef]
61. Griffiths, B.S.; Ritz, K.; Bardgett, R.D.; Cook, R.; Christensen, S.; Ekelund, F.; Sørensen, S.J.; Bååth, E.; Bloem, J.; De Ruiter, P.C.; et al. Ecosystem response of pasture soil communities to fumigation-induced microbial diversity reductions: An examination of the biodiversity-ecosystem function relationship. *Oikos* **2000**, *90*, 279–294. [CrossRef]
62. Okada, H.; Harada, H.; Kadota, I. Application of diversity indices and ecological indices to evaluate nematode community changes after soil fumigation. *Nematol. Res.* **2004**, *34*, 89–98. [CrossRef]
63. Yeates, G.W. Nematodes as soil indicators: Functional and biodiversity aspects. *Biol. Fert. Soils* **2003**, *37*, 199–210. [CrossRef]
64. Stirling, G.; Wilsey, B. Empirical relationships between species richness, evenness, and proportional diversity. *Am. Nat.* **2001**, *158*, 286–299. [CrossRef]
65. Bardgett, R.D.; van der Putten, W.H. Belowground biodiversity and ecosystem functioning. *Nature* **2014**, *515*, 505–511. [CrossRef]

Testimonial Letter 1: University of California

University *of* California
Agriculture and Natural Resources

UC Cooperative Extension-Kern County

1031 S. Mt. Vernon Avenue
Bakersfield, CA 93307-2851
661-868-6200 office
661-868-6208 fax
cekern@ucdavis.edu
http://cekern.ucdavis.edu

December 9, 2019

TO WHOM IT MAY CONCERN,

RE: Benefits Discussion for Fluensulfone (brand name NIMITZ®) Use in the production of numerous specialty crops and minor uses.

I am an emeritus vegetable farm advisor for the University of California Cooperative Extension. I'm writing in support of Nimitz (f*luensulfone*) for use on the minor crops registered within this product. As the UCCE vegetable farm advisor in Kern County I routinely evaluate products that may have a benefit to the vegetable growers in California and Kern County in particular. I have trialed this product extensively on carrots and tomatoes for over five years. We have found Nimitz to perform remarkably well in the control of nematodes.

Fluensulfone is a pyrazole nematicide and is the first nematicide in the fluoroalkenyl class. Fluensulfone has activity activity against nematodes that includes weak inhibition of motility in adults, strong inhibition of motility in larvae, feeding inhibition and egg-laying, hatching and developmental inhibition. Inhibition of larval thrashing and feeding is irreversible after 24 hours of exposure and the cuticle does not appear to prevent access of fluensulfone. It targets Root-knot (*Meloidogyne* spp.), Potato cyst (*Globodera* spp.), Needle (*Longidorus africanus*), Lance (*Hoplolaimus* spp.), Sting (*Belonolaimus* spp.), stubby root (*Trichodorus* and *Paratrichodorus* spp.), and Lesion (*Pratylenchus* spp.).

Fluensulfone, unlike other chemical controls, presents with relatively low toxicity to non-target organisms. In addition to that, this soil applied nematicide is easier to apply than current available tool such as fumigants.

We tested fluensulfone to control root-knot nematode (*Meloidogyne* spp.) on carrots and tomatoes. Results were favorable in that they showed a significant marketable yield increase with fluensulfone as compared to non-treated controls. Fluensulfone also caused a significant decrease in root-knot nematodes in infested carrots and tomatoes. The results from my trials has been reported to the California Tomato Research Institute and California Fresh Carrot Advisory Board. I have reported these findings to many grower meetings throughout California and my presentations and newsreleases on these trials are widely available online.

Carrots are particularly vulnerable to nematode injury because the root is the product that is marketed. Carrots essentially have a zero tolerance to nematode injury. The primary plant parasitic nematode that effects vegetable crops in California is root-knot nematodes (*Meloidogyne spp.*) Products like Nimitz are very important to all vegetable production practices but especially for carrot production.

Fluensulfone provides growers with an effective tool to combat problematic species of: root-knot nematode (*Meloidogyne* .). Fluensulfone offers increased opportunity for integrated approaches to be used for both pest and soil nutrient management programs when compared to other currently registered alternatives. This new nematicide product is selective for nematodes relative to older chemistries such as fumigants and oxamyl, which will allow growers increased flexibility in using them and opportunities for increased soil nutrient management and integrated pest management techniques to be practiced. Fluensulfone offers a more flexible and selective tool that increases a grower's capacity to practice field management strategies that better promote beneficial bacteria, earthworms, and insect populations contributing to strong IPM programs and more sustainable stewardship practices. Thank you for your consideration.

Sincerely,

Joe Nunez
Vegetable/Plant Pathology Farm Advisor
University of California Cooperative Extension
1031 South Mount Vernon Ave.
Bakersfield CA 93307

Testimonial Letter 2: University of California, Davis

UNIVERSITY OF CALIFORNIA, DAVIS

BERKELEY • DAVIS • IRVINE • LOS ANGELES • MERCED • RIVERSIDE • SAN DIEGO • SAN FRANCISCO SANTA BARBARA • SANTA CRUZ

DEPARTMENT OF ENTOMOLOGY AND NEMATOLOGY
COLLEGE OF AGRICULTURAL AND ENVIRONMENTAL SCIENCES
ONE SHIELDS AVENUE
DAVIS, CA 95616
(530) 752-2215 OFFICE
(530) 754-9077 FACSIMILE

December 16, 2019

RE: Benefits Discussion for Fluensulfone (brand name NIMITZ®, previously known as MCW-2) Use in the production of numerous specialty crops and minor uses.

I am writing in support of the continued use of Nimitz for the production of specialty crops and minor uses. This letter represents my personal views and experiences as a University of California Cooperative Extension Specialist in nematology, and not those of the University of California.

Plant parasitic nematodes represent a chronic problem for growers. Nimitz has become an essential component in our efforts to develop IPM programs for growers, as well as the development of alternatives to the use of fumigant nematicides on annual crops. Since 2010, I have conducted more than 30 field research trials evaluating the effectiveness of Nimitz (previously known as MCW-2) against root-knot nematode (*Meloidogyne* sp). This includes trials on carrots (7 trials), cantaloupe (5 trials), pepper (2 trials), strawberry (3 trials), cucumber (6 trials), squash (3 trials), tomato (4 trials), eggplant (2 trials), and onion (1 trial). These trials have shown Nimitz to be a very effective and consistent product for preplant treatment, providing both increases in yield, and reductions in nematode populations. Two peer reviewed publications with Nimitz (MCW-2) are included with this letter.

Fluensulfone, the active ingredient of Nimitz, represents not only a new mode of action for a nematicide, but one that has relatively low toxicity to non-target organisms compared to earlier generations of products. This also makes the product much safer for use by growers, applicators, and field personnel. The ability to have and utilize products with diverse modes of action is an essential component of IPM programs and is necessary to minimize development of resistance.

For the above reasons, I support the continued use of Nimitz for the production of specialty crops and minor uses. In case more information is needed, please don't hesitate to contact me.

Sincerely,

Becky B. Westerdahl

Becky B. Westerdahl
Extension Nematologist / Professor
Phone: 530-320-7213, Email: bbwesterdahl@ucdavis.edu

Testimonial Letter 3: Michigan State University

MICHIGAN STATE UNIVERSITY

December 16, 2019

Miriam Frugis
Federal Regulatory Manager
ADAMA <miriam.frugis@adama.com>;

RE: Benefits Discussion for Fluensulfone (brand name NIMITZ®) Use in the production of numerous specialty crops and minor uses.

As an applied agricultural nematologist in the process of retiring, during the past five years I have had several research projects involving Fluensulfone (NIMITZ®) on both specialty and agricultural crops grown under Michigan conditions. The specialty crops included work with carrots, apples and grapes. The carrot work was related to control of a very aggressive population of *Pratylenchus penetrans* (Penetrans root-lesion nematode), while the apple and grape research related to the impact of fluensulfone on soil health as measured through nematode community structure.

In the carrot research, fluensulfone resulted an excellent improvement of overall carrot quality and yield. The nematode community structure research associated with both apples and grapes showed no negative impact on overall soil health.

Kindly do not hesitate to contact me if I can be of additional assistance in your documentation of the benefits of NIMITZ on specialty crops.

Sincerely,

George W. Bird
birdg@msu.edu

cc Pablo Navia Gine, pablo.navia@adama.com

College of Agriculture and Natural Resources

Department of Entomology

288 Farm Ln Rm 243
East Lansing, MI 48824

517-355-4663
Fax: 517-432-7061
www.ent.msu.edu

MICHIGAN STATE UNIVERSITY

December 16, 2019

To: Pablo Navia Gine
East Region Development Leader ADAMA US
3120 Highwoods Blvd, Suite 100
Raleigh, NC 27604
Cell: 229-256-7762
Email: pablo.navia@adama.com

Dear Pablo,

We have conducted several trials that include Nimitz in potatoes, carrots, and parsnips. Our trials have been conducted in growers fields in Michigan and were all randomized block design replicated trials.

In the trials that had high numbers of Northern Root Knot Nematodes, Nimitz was our most effective product. We are happy to continue working with your excellent products.

Sincerely,

Marisol Quintanilla

Marisol Quintanilla, Ph.D.

Applied Nematologist
Department of Entomology
Natural Science Building
Michigan State University
288 Farm Lane Room 51
East Lansing, MI 48824

Office: 517-884-2058
Cell: 517-881-3740
Email: marisol@msu.edu

Testimonial Letter 4: Wilbur Ellis Company

December 9, 2019

TO WHOM IT MAY CONCERN,

RE: Benefits Discussion for Fluensulfone (brand name NIMITZ®) Use in the production of numerous specialty crops and minor uses.

Wilbur Ellis is a leader in servicing the agricultural community for over 75 years nationwide, and has been in the Coachella Valley since 1999. Their expertise in managing the many crops grown have made them an expert in the valley. I have been working with Prime Time International for over twenty years managing their main commodity, bell peppers.

Fluensulfone is a pyrazole nematicide and is the first nematicide in the fluoroalkenyl class. Fluensulfone has activity activity against nematodes that includes weak inhibition of motility in adults, strong inhibition of motility in larvae, feeding inhibition and egg-laying, hatching and developmental inhibition. Inhibition of larval thrashing and feeding is irreversible after 24 hours of exposure and the cuticle does not appear to prevent access of fluensulfone. It targets Root-knot (*Meloidogyne* spp.), Potato cyst (*Globodera* spp.), Needle (*Longidorus africanus*), Lance (*Hoplolaimus* spp.), Sting (*Belonolaimus* spp.), stubby root (*Trichodorus* and *Paratrichodorus* spp.), and Lesion (*Pratylenchus* spp.).

Fluensulfone, unlike other chemical controls, presents with relatively low toxicity to non-target organisms. In addition to that, this soil applied nematicide is easier to apply than current available tool such as fumigants.

We tested fluensulfone to control root knot nematodes on bell peppers. Results were favorable in that nematodes were controlled and showed positive yield benefits. Nimitz controlled about 70% of the nematode population that was present.

Fluensulfone provides growers with an effective tool to combat problematic species of: root-knot (Meloidogyne spp.) and stubby-root nematode (Trichodorus spp.). Fluensulfone offers increased opportunity for integrated approaches to be used for both pest and soil nutrient management programs when compared to other currently registered alternatives. This new nematicide product is selective for nematodes relative to older chemistries such as fumigants and oxamyl, which will allow growers increased flexibility in using them and opportunities for increased soil nutrient management and integrated pest management techniques to be practiced. Fluensulfone offers a more flexible and selective tool that increases a grower's capacity to practice field management strategies that better promote beneficial bacteria, earthworms, and insect populations contributing to strong IPM programs and more sustainable stewardship practices.

Thank you for your consideration.

Sincerely,

Paul Darroch

Paul Darroch, Pest Control Advisor, Wilbur Ellis Company

Testimonial Letter 5: University of Florida

UF|IFAS
UNIVERSITY *of* FLORIDA

Gulf Coast Research and Education Center

14625 CR 672
Wimauma, FL 33598
Ph: 813-634-0000
Fax: 813-634-0001
http://gcrec.ifas.ufl.edu/

Date: 12/16/2019

TO WHOM IT MAY CONCERN,
RE: Benefits Discussion for Fluensulfone (brand name NIMITZ®) Use in the production of numerous specialty crops and minor uses.

I am a nematologist at the University of Florida with a focus on integrated nematode management in fruits and vegetable, and as such conduct many field trials evaluating new nematode management products and practices.

Fluensulfone is one of the products I have worked with a lot in recent years. Fluensulfone is a new pyrazole nematicide,that has very specific activity against nematodes. Its activity includes inhibition of motility, feeding, egg-laying, hatching and overall development. It targets most of the plant-parasitic nematodes, including root-knot (*Meloidogyne* spp.), potato cyst (*Globodera* spp.), needle (*Longidorus africanus*), lance (*Hoplolaimus* spp.), sting (*Belonolaimus* spp.), stubby root (*Trichodorus* and *Paratrichodorus* spp.), and lesion (*Pratylenchus* spp.).
Fluensulfone, unlike older nematicides and soil fumigants, has low mammalian toxicity, and relatively low toxicity to non-target organisms, and is easy to apply.

We tested fluensulfone to control root-knot nematodes on several vegetable crops, including tomato, pepper, cucumber, squash, cantaloupe and watermelon. In addition, we also evaluated the product to control sting, root-knot and lesion nematodes in strawberries. Our results showed that this material has good potential to help manage nematodes in Florida. The product provides growers with a new and much safer tool to combat problematic nematode species, especially root-knot nematodes, the most problematic nematodes in Florida. Fluensulfone offers a new opportunity for integrated nematode management approaches. This is especially important in Florida, where nematode management primarily relies on soil fumigants.This new nematicide is much safer to applicators, and highly selective towards nematodes, unlike older chemistries such as fumigants and oxamyl. Fluensulfone therefore offers a more flexible and selective nematode management tool which increases a grower's capacity to practice field management strategies that better promote soil health, and could lead to more sustainable soil management practices.

UF|IFAS
UNIVERSITY *of* FLORIDA

Gulf Coast Research and Education Center

14625 CR 672
Wimauma, FL 33598
Ph: 813-634-0000
Fax: 813-634-0001
http://gcrec.ifas.ufl.edu/

Thank you for your consideration.

Sincerely,

Johan Desaeger
Assistant Proferssor Nematology
Gulf Coast Research and Education Center UF/IFAS
14625 CR 672
Wimauma, FL 33598
Tel 813-419-6592 office/ 813-431-6246 cell

Testimonial Letter 6: Loot Farms

Date: December 13,2019

TO WHOM IT MAY CONCERN,

RE: Benefits Discussion for Fluensulfone (brand name NIMITZ®) Use in the production of numerous specialty crops and minor uses.

Fluensulfone unlike other chemical controls, has relatively low toxicity to non-target organisms. In addition to that, this soil applied nematicide is easier to apply than other current nematicides such as fumigants.
We tested fluensulfone to control Root nematodes (*Meloidogyne spp*) on the crop
Bitter Melon

Fluensulfone , a non-fumigant and non-restricted use nematicide, allows us to grow Bitter Melons. Fumigants are not an option for us due to our proximity to urban settings. **Also, it is an effective tool to combat problematic species of:** Root nematodes (*Meloidogyne spp.*).

For us at Loot Farms, Fluensulfone offers a more flexible and selective tool that increases a grower's capacity to practice field management strategies. These in turn, help to better promote beneficial bacteria, earthworms, and insect populations which contribute to strong IPM programs and more sustainable stewardship practices.

Thank you for your consideration.

Sincerely,

Harry Grafe
Loot Farms
Cell (786) 255-4154

Testimonial Letter 7: Kiwifruit Administrative Committee

Kiwifruit
Administrative Committee

December 16, 2019

TO WHOM IT MAY CONCERN,

RE: Benefits Discussion for Fluensulfone (brand name NIMITZ®) Use in the production of numerous specialty crops and minor uses.

The Kiwifruit Administrative Committee is the kiwifruit industry representative organization that sets and enforces regulatory standards for all kiwifruit produced in the United States and imported kiwifruit to ensure that minimum grades and standards are met. The organization funds marketing and research efforts to the benefit of the industry and funded trial research on Fluensulfone for treatment of root-knot nematodes in partnership with one of the Kiwifruit Administrative Committee's industry partners, Sun Pacific. Effective nematode control is currently a significant challenge to California kiwifruit growers as available treatments are not efficacious.

Fluensulfone is a pyrazole nematicide and is the first nematicide in the fluoroalkenyl class. Fluensulfone has activity activity against nematodes that includes weak inhibition of motility in adults, strong inhibition of motility in larvae, feeding inhibition and egg-laying, hatching and developmental inhibition. Inhibition of larval thrashing and feeding is irreversible after 24 hours of exposure and the cuticle does not appear to prevent access of fluensulfone. It targets Root-knot (*Meloidogyne* spp.), Potato cyst (*Globodera* spp.), Needle (*Longidorus africanus*), Lance (*Hoplolaimus* spp.), Sting (*Belonolaimus* spp.), stubby root (*Trichodorus* and *Paratrichodorus* spp.), and Lesion (*Pratylenchus* spp.).

Fluensulfone, unlike other chemical controls, prevents with relatively low toxicity to non-target organisms. In addition to that, this soil applied nematicide is easier to apply than currently available tools such as fumigants.

During the trail research conducted by Sun Pacific, the percent soil nematode population change (NPC) in July for Nimitz treatments (12.7%) was significantly less than the untreated control (101.9%). These study results indicate control of soil nematode population in the Nimitz treatments as they did not change significantly from May to July. By comparison, the soil nematode population in the untreated control increased substantially from May to July. The Nimitz treatment controlled the nematode population compared to the untreated control more than 85% approximately 9 weeks after the first split application.

Similarly, in September, the Nimitz treatments reduced the nematode population compared to the untreated control by about 50% or more 16 weeks after the first split Nimitz application and 9 weeks after the second split application. These results indicate that the soil nematode population in the Nimitz treatments moderately increased by September, while the soil nematode population of the untreated control strongly increased from May to September.

1521 "I" Street
Sacramento, CA 95814
t 916.441.0678
f 916.446.1063
www.kiwifruit.org

The NPC was significantly less (p=0.05) in plots treated with the highest rate of Nimitz (5.6 pt/acre) compared to the untreated control at both the July and September timings. These data show that the Nimitz 5.6 pt/acre rate controlled the nematode population compared to the untreated control over 95% between May and July and 75% between July and September.

Fluensulfone provides growers with an effective tool to combat problematic species of: root-knot (Meloidogyne spp.). Fluensulfone offers increased opportunity for integrated approaches to be used for both pest and soil nutrient management programs when compared to other currently registered alternatives.

This new nematicide product is selective for nematodes relative to older chemistries such as fumigants and oxamyl, which will allow growers increased flexibility in using them and opportunities for increased soil nutrient management and integrated pest management techniques to be practiced. Fluensulfone offers a more flexible and selective tool that increases a grower's capacity to practice field management strategies that better promote beneficial bacteria, earthworms, and insect populations contributing to strong IPM programs and more sustainable stewardship practices.

Kiwifruit growers greatly need alternative treatments for nematode control like Nimitz.

Sincerely,

Nicholas Matteis, Assistant Manager

Testimonial Letter 8: Grow West

GROW
WEST
201 East Street, Woodland, CA 95776

December 9, 2019

TO WHOM IT MAY CONCERN,

RE: Benefits Discussion for Fluensulfone (brand name NIMITZ®) Use in the production of numerous specialty crops and minor uses.

Grow West is a retail agricultural supply company located in Northern California. Grow West services all crops grown in this region. In addition, we have established a technical service department to aid our pest control advisors in understanding new technologies. It is in this capacity that we have had the opportunity to evaluate Nimitz for lesion nematode activity in walnuts

Fluensulfone is a pyrazole nematicide and is the first nematicide in the fluoroalkenyl class. Fluensulfone has activity activity against nematodes that includes weak inhibition of motility in adults, strong inhibition of motility in larvae, feeding inhibition and egg-laying, hatching and developmental inhibition. Inhibition of larval thrashing and feeding is irreversible after 24 hours of exposure and the cuticle does not appear to prevent access of fluensulfone. It targets Root-knot (*Meloidogyne* spp.), Potato cyst (*Globodera* spp.), Needle (*Longidorus africanus*), Lance (*Hoplolaimus* spp.), Sting (*Belonolaimus* spp.), stubby root (*Trichodorus* and *Paratrichodorus* spp.), and Lesion (*Pratylenchus* spp.).

Fluensulfone, unlike other chemical controls, presents with relatively low toxicity to non-target organisms. In addition to that, this soil applied nematicide is easier to apply than current available tool such as fumigants.

We tested fluensulfone to control lesion nematode (*Pratylenchus* spp.) on walnut. Over the years of testing, results have been favorable. Fluensulfone has shown to decrease nematode counts.

Fluensulfone provides growers with an effective tool to combat problematic species of: lesion nematode (*Pratylenchus* spp.) Fluensulfone offers increased opportunity for integrated approaches to be used for both pest and soil nutrient management programs when compared to other currently registered alternatives. This new nematicide product is selective for nematodes relative to older chemistries such as fumigants and oxamyl, which will allow growers increased flexibility in using them and opportunities for increased soil nutrient management and integrated pest management techniques to be practiced. Fluensulfone offers a more flexible and selective tool that increases a grower's capacity to practice field management strategies that better promote beneficial bacteria, earthworms, and insect populations contributing to strong IPM programs and more sustainable stewardship practices.
Thank you for your consideration.

Sincerely,
Matt Ehlhardt

Matt Ehlhardt
Director of Technical Service
Grow West