TITLE

Oxathiapiprolin Petition for an Extension of the Exclusive Use Period as Permitted by FIFRA Section 3(c)(1)(F)(ii)

TEST GUIDELINE

FIFRA Section 3(c)(1)(F)(ii)

AUTHOR

Brian L. Bret, PhD

STUDY COMPLETION DATE

24 March 2022

STUDY SPONSOR

Corteva Agriscience LLC
9330 Zionsville Road
Indianapolis, IN 46226

PERFORMING LABORATORY

Not applicable

STUDY ID

Not applicable

PAGES

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STATEMENT OF NO DATA CONFIDENTIALITY CLAIMS

Compound: oxathiapiprolin

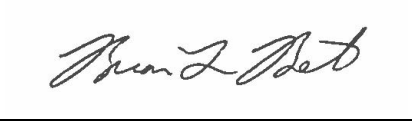
Title: Oxathiapiprolin Petition for an Extension of the Exclusive Use Period as Permitted by FIFRA Section 3(c)(1)(F)(ii)

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

Company: Corteva Agriscience LLC

Company Agent: Brian L. Bret, PhD

Title: US Regulatory Leader

Signature 

Date: 24 March 2022

THESE DATA MAY BE CONSIDERED CONFIDENTIAL IN COUNTRIES OUTSIDE THE UNITED STATES

STATEMENT OF COMPLIANCE WITH GOOD LABORATORY PRACTICE STANDARDS

Compound: oxathiapiprolin

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This report does not meet the definition of a GLP study as it appears in:

United States Environmental Protection Agency
Title 40 Code of Federal Regulations Part 160
Federal Register, 17 August 1989

Organization for Economic Cooperation and Development
ENV/LMC/CHEM(98)17, Paris – January 26, 1998

NON-GLP STUDY

Corteva Agriscience LLC	24 March 2022
Sponsor Company	Date

Corteva Agriscience LLC	24 March 2022
Submitter Company	Date

Corteva Agriscience LLC	24 March 2022
Study Director Company	Date

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1.0 EXECUTIVE SUMMARY

The active ingredient oxathiapiprolin is a fungicide with a novel mode of action developed by Corteva Agriscience, LLC (formerly DuPont Crop Protection). Corteva Agriscience, LLC and Syngenta Crop Protection have a supply and data access agreement in the United States and Canada. Oxathiapiprolin is the only currently registered member of the Fungicide Resistance Action Committee (FRAC) Group 49 (formerly U15) with target site code F9 lipid homeostasis and transfer/storage. Thus, oxathiapiprolin plays a vital role in resistance management by providing a highly effective rotation partner for other fungicides.

Oxathiapiprolin provides excellent disease control for certain oomycete diseases (*Phytophthora* spp. and downy mildew) in agricultural crops, turf, and ornamentals. It is a systemic fungicide and moves systemically in the plant xylem. Uptake into the leaf tissue allows good translaminar movement and protection of new plant growth. Oxathiapiprolin is generally applied 2 to 4 times per growing season via soil or foliar, but not both, at a single application rate for the U.S. use pattern ranging from 0.01 to 0.25 lb ai/A. The maximum season application rates on crops in the U.S. ranges between 0.125 lb a.i./A/year for most foliar applications and 0.50 lb a.i./A/year for soil applications with Pre-harvest intervals (PHI) ranging from 0 to 14 days. A minimum 3 to 14 day retreatment interval is based on crop and pest.

According to EPA Decision Memorandum[1] dated August 27, 2015, the EPA determined oxathiapiprolin met the criteria for Reduced Risk status for all food and non-food uses for which that status has been sought (MRID 49033238). Due to the lack of toxicity observed in the oxathiapiprolin database, toxicological end points and points of departure (POD) were not established, and EPA conducted a qualitative risk assessment. There is no evidence of carcinogenicity in cancer studies and EPA classified oxathiapiprolin as "not likely to be carcinogenic to humans"[2]. Potential exposure to oxathiapiprolin during mixing, loading, and spraying does not involve a significant risk to the health of operators when appropriate standard work clothing is utilized. Oxathiapiprolin demonstrates a favorable environmental fate profile due to low water solubility and high binding coefficients and demonstrates a favorable toxicity profile for non-target aquatic and terrestrial organisms among many of the competitive fungicides.

Per FIFRA section 3(c) (1) (F) (ii), the exclusive use period may be extended if new minor uses are registered within the first 7 years of the commencement of the exclusive use period, which is the case with oxathiapiprolin. In addition, the new uses must meet at least one of the four criteria outlined in FIFRA section 3(c) (1) (F) (ii). For each 3 minor uses registered within this timeframe that meet the necessary standards, the exclusive use period may be extended for 1

[1] EPA-HQ-OPP-2014-0114-0026 Registration Decision for the New Active Ingredient Oxathiapiprolin.
[2] EPA-HQ-OPP-2014-0114-0006 Human Health Risk Assessment

year. In this document, justification is provided for extending the exclusive use period of oxathiapiprolin by three years (registered on at least 9 minor crops, each <300,000 acres).

When determining the number of minor uses within a crop group, FIFRA 3(c)(1)(F)(ii) states that, *"the registration of a pesticide for a minor use on a crop grouping established by the Administrator shall be considered for purposes of this clause 1 minor use for each representative crop for which data are provided in the crop grouping*." That is, one minor use may be credited for each representative crop for which residue trial data were submitted on a one-for-one basis.

Thirteen (13) minor uses can be found spread across multiple Corteva and Syngenta commercial labels listed in Table 1. Corteva believes that the oxathiapiprolin uses cited in this petition qualify as minor uses based on acres harvested in the USDA National Agricultural Statistics Service (NASS) 2017 census (Summarized in Table 2).

Table 1. Oxathiapiprolin Product Registrations

Product	EPA Reg No	Most Recent Label Accepted Date	Registration Status
DPX-TAH88 MUP	352-930	Oct 02, 2020	Registered (Oct 02, 2020)
Dupont Lumisena	352-920	Nov 20, 2020	Registered (Nov 14, 2016)
Dupont Zorvec Enicade	352-891	Aug 14, 2017	Registered (Aug 31, 2015)
Dupont Zorvec Epicaltrin	352-892	Aug 14, 2017	Registered (Aug 31, 2015)
Zorvec Technical	352-890	Aug 14, 2017	Registered (Aug 31, 2015)
Lumisena	352-920	Nov 30, 2020	Registered (Nov 14, 2016)
Orondis Gold 200	100-1571	Aug 17, 2020	Registered (Sep 10, 2015)
Orondis Opti A	100-1572	Oct 05, 2017	Registered (Sep 10, 2015)
Orondis Ultra A	100-1572	Oct 05, 2017	Registered (Sep 10, 2015)
Oxathiapiprolin FHG OD	100-1532	Aug 28, 2017	Registered (Aug 31, 2015)
Oxathiapiprolin FHG SC	100-1533	Aug 28, 2017	Registered (Aug 31, 2015); Inactive
Orondis	100-1571	Aug 17, 2020	Registered (Sep 10, 2015)
Orondis	CA200001	Jun 16, 2020	Registered (Jun 16, 2020)
Orondis Gold	100-1614	Nov 13, 2020	Registered (Mar 03, 2017)
Orondis OD	100-1572	Oct 05, 2017	Registered (Sep 10, 2015)
Orondis OD	MI160002		Registered (Mar 16, 2017)
Orondis Opti	100-1591	Nov 08, 2021	Registered (Sep 07, 2016)
Orondis Technical	100-1624	Aug 17, 2020	Registered (Aug 07, 2017)
Orondis Ultra	100-1612	Aug 17, 2020	Registered (Feb 03, 2017)
Oxathiapiprolin 20SC MUP	352-924	Aug 17, 2020	Registered (Oct 18, 2017)
Plenaris 200FS	100-1590	Aug 28, 2017	Registered Nov 14, 2016)
Segovis	100-1533	Aug 28, 2017	Registered (Aug 31, 2015)
Zorvec Technical	352-890	Aug 17, 2020	Registered (Aug 31, 2015)
Zorvec Encantia	352-930	Oct 02, 2020	Registered (Oct 02, 2020)

Source: USEPA Pesticide Product and Label System
https://ordspub.epa.gov/ords/pesticides/f?p=PPLS:1

2.0 CRITERIA MET PER FIFRA SECTION 3(C) (1) (F) (II)

According to the US Federal Insecticide Fungicide and Rodenticide Act (FIFRA), only one of the four following criteria must be met to qualify a minor use registration toward extension of the exclusive use data period:

1. There are insufficient efficacious alternative registered pesticides available for the use;
2. The alternatives to the minor use pesticide pose greater risks to the environment or human health;
3. The minor use pesticide plays or will play a significant part in managing pest resistance;
4. The minor use pesticide plays or will play a significant part in an integrated pest management program.

Oxathiapiprolin, as detailed below, meets at least one or more of the four criteria for all 13 minor crops cited in this petition.

Criteria #1, insufficient efficacious alternative registered pesticides available for the use, is met for oxathiapiprolin on the currently-registered minor crops below (Table 2). For each crop listed, data supporting Criteria 1 is provided from IR-4's Food Request Database (https://ir4app.cals.ncsu.edu/Ir4FoodPub/fullSearchResult), internal market analysis/trial data, and/or peer-reviewed publications. A more detailed example using pomegranate is provided below in the Case Study in Section 4.0. For certain crops, the IR4 requestor(s) also note oxathiapiprolin's value in resistance management which satisfies **Criteria 3, the minor use pesticide plays or will play a significant part in managing pest resistance** and its utility in an IPM program, which satisfies **Criteria 4, the minor use pesticide plays or will play a significant part in an integrated pest management program.**

Table 2. Acres harvested per year for registered minor use crops and data supporting satisfaction of Criteria 1 and/or Criteria 4 per FIFRA section 3(c) (1) (F) (ii).

Crop Group or Subgroup	Registered Minor Use Crop	Acres Harvested per year	Supporting data/comments
Berries; Bushberry, Crop Subgroup 13B	blueberry, highbush	153,258	Similar to caneberry, bushberry (blueberry) crops are susceptible to root rot (*Phytophthora spp*.) with very few options to treat. Metalaxyl, mefenoxam and phosphites are widely used to treat the disease with no other rotational products currently labeled that offer control of the disease. Oxathiapiprolin is an excellent IPM fit, thus also satisfying **Criteria 4** that offers growers a new mode of action and rotational partner for control of this disease, which satisfies **Criteria 3**.
Berries; Low-growing berry	strawberry	60,162	Per IR4 PR# 11719, oxathiapiprolin was requested to control *Phytophthora spp.* (Leather Rot, Red Stele, Crown

subgroup, Crop Subgroup 13-07G			Rot). Root rot is described as a “widespread problem in strawberries” and the request came from numerous states: CA, FL, LA, MI, OR, and VA. The comments from requestors also list additional benefits, satisfying **Criteria 3** and **Criteria 4**: “Very good IPM fit; AI has a different mode of action and is needed for resistance management.”
Caneberry Crop Subgroup 13-07A	blackberry	16,671	Per IR4 PR# 11720, oxathiapiprolin was requested by cooperators in VA, OR and CA to control Root Rot, described as “widespread, causing significant yield/economic losses”. The request also indicates the need for alternative treatments for these diseases is even more important due to losing effective fumigants. The IR4 requests also indicates **Criteria 3** and **Criteria 4** are satisfied because oxathiapiprolin is a “very good IPM fit; AI has different mode of action and is needed for resistance management”.
Citrus Crop Group 10-10	lemon, grapefruit tangerine	66,501 68,390 77,701	*Phytophthora* spp. are a significant problem for citrus growers in FL and CA, resulting in tree decline and death. This pathogen has few management options (at the time of oxathiapiprolin registration in this crop, growers had and option of phosphites, metalaxyl or mefenoxam). All options have been registered for some time and have resistance concerns (Adaskaveg 2020a). Thus, oxathiapiprolin offered a new mode of action and rotational product for resistance management, satisfying **Criteria 3** as well.
Citrus Crop Group 10-10	orange, post-harvest	NA	Per IR4 PR# 11312, oxathiapiprolin was requested by CA because it “provides long residual disease control” for brown rot. Request also indicates **Criteria 3** and **Criteria 4** are satisfied: “Product fits well in IPM as it is specific to oomycetes, is a new mode of action for resistance management”.
Herb, Fresh Leaves Subgroup 13A	basil	NA	Per IR4 PR#10772 and 10881, oxathiapiprolin was requested by cooperators in MI, HI, NC, FL, NY, and CA to control Downy mildew which was described as “becoming more common and can result in significant damage to basil crops”. Patel et al. 2015: "Downy mildew has become the most devastating foliar disease in basil and is now a major limiting factor for basil production in the United States. Strategies for management of basil downy mildew are very limited owing to the fact that the disease was found so recently, the lack of host resistance in commercially grown sweet basil, and the scarcity of choices of effective fungicides currently registered on basil."

Hops, Miscellaneous Commodity	hops	59,429	Per IR4 Priority Setting Tool and Comments (PR# 11759): "Downy mildew: *Pseudoperonospora humuli*. Hops production has expanded into US regions that are wet and humid resulting in significant downy mildew outbreaks. A Crisis was declared in MI in 2015 as a result of disease pressure." Requests were made for oxathiapiprolin registration on hops from university cooperators in OR, NC, and MI.
Stalk and Stem Vegetables, Crop Subgroup 22A	asparagus,	29,907	Per IR4 Priority Setting Tool (PR# 10623): "Request is for *Phytophthora spp*, which is a disease of asparagus in Michigan where it is a bad problem." This use was also requested again for asparagus by Dr. Mary Hausbeck (MI) in a separate food request (PR# 10618) which demonstrates the need for efficacious alternatives and interest from growers.
Tree Nut, Crop Group 14-12	Hazelnut, Macadamia Nut	70,091 18,403	*Phytophthora* root rot can significantly impact and kill young or bearing trees with the only options growers have to treat is fumigation (prior to planting) or use of phosphites, metalaxyl or mefenoxam products until registration of oxathiapiprolin in late 2020. Over-reliance on phosphite and mefenoxam based products can lead to resistance and poor performance, thus oxathiapiprolin also addresses **Criteria 3** by offering a rotational option for resistance management.
Tropical and Subtropical Fruit, Medium to large fruit, smooth inedible peel, Crop Subgroup 24B	Avocado, pomegranate	64,455 31,472	Per IR4 Priority Setting Tool and Comments (PR# 11795): "Management of *Phytophthora* root [rot] is a major problem; trunk injections of phosphites create wounds that attract shot hole borers [therefore] chemigation treatments are needed to manage root rot and trunk cankers by lowering inoculum levels." [See Case Study in Section 4.0.] Also meets **Criteria 3** and **Criteria 4**; Per IR4 Priority Setting Tool and Comments (PR# 11795): "Very good IPM fit; use very low rates and helps with replacing phosphite trunk injection injuries; provides rotational product with phosphite soil application."

Criteria #2, alternatives to the minor use pesticide pose greater risks to the environment or human health, is met for the minor crops cited herein because:

- Oxathiapiprolin is classified as "not likely to be a human carcinogen".
- Due to the limited toxicity of oxathiapiprolin, EPA did not establish acute or chronic toxicity endpoints and points of departure for quantitative risk assessment and conducted

a qualitative human health risk assessment, thus providing the highest margins of safety for operators and bystanders.

- Acute and chronic dietary reference doses (aRfD and cRfD) were not established by EPA for oxathiapiprolin because of limited toxicity.
- Potential exposure to oxathiapiprolin during mixing, loading, and spraying does not involve a significant risk to the health of operators when appropriate standard work clothing is utilized.

Criteria #3, the minor use pesticide plays or will play a significant part in managing pest resistance, is met for currently-registered minor crops cited in this petition as indicated in Table 2. Oxathiapiprolin is the only currently registered member of the Fungicide Resistance Action Committee (FRAC) Group 49 (formerly U15) with target site code F9 lipid homeostasis and transfer/storage. Many of the crops listed above are susceptible to root rot disease caused by *Phytophthora spp.* There are currently very few products that are labeled for control of these pathogens, most commonly phosphites, metalaxyl and mefenoxam are used for disease control. However, limited options usually result in resistance such has been reported in tree nuts (Adaskaveg, 2020b) and citrus (Adaskaveg, 2020a) as well as many other crops. Thus, oxathiapiprolin plays a vital role in resistance management by providing a highly effective rotation partner for other fungicides (Cohen et al 2018).

Criteria #4, the minor use pesticide plays or will play a significant part in an integrated pest management program, is also met for currently-registered minor crops cited in this petition as indicated in Table 2. The combination of excellent efficacy, crop safety, low human health risk, low environmental risk, and value as a resistance management rotation partner make oxathiapiprolin a valuable fungicide management tool in IPM programs.

3.0 CONCLUSION

The 13 registered minor use crops detailed above as described by IR-4 minor crop requestors, grown on ≤ 300,000 acres, are shown to meet one or more of the 4 criteria as defined per FIFRA section 3(c) (1) (F) (ii) (Table 4). Therefore, Corteva affirms that more than 9 minor crop uses exist to qualify oxathiapiprolin for the 3-year exclusive-use extension from the initial Zorvec Technical (352-890) registration date of 31 August 2015.

4.0 APPENDIX 1: CASE STUDY: IMPACT OF PHYTOPHTHORA ROOT ROT DISEASE CONTROL ON POMEGRANATE

Author (s): Katie Neufeld, PhD

Completion Date: December 2021

Sponsor: Syngenta Crop Protection, LLC
410 Swing Road
Post Office Box 18300
Greensboro, NC 27419-8300 USA

Phytophthora root rot is a disease caused by *Phytophthora spp.* which impacts the roots, stems and branches of many different crops, including pomegranate. A multi-year study in pomegranate was conducted by Syngenta in Pauma Valley, CA. The orchard of pomegranates were grown in the basin of foothills with an avocado orchard situated on the hillside. The avocados provided continual *Phytophthora cinnamomi* inoculum when rainfall ran into the pomegranate orchard from the hillside.

Trees in the study were treated twice in 2020 and again in 2021 with either oxathiapiprolin (Orondis®) or mefenoxam (Ridomil® Gold). Mefenoxam is not labeled for use in pomegranate, however it is an industry standard in other perennial crops such as almonds and citrus, thus used as a standard in this study. Oxathiapiprolin controls *Phytophthora* propagules as well as or better than mefenoxam, with far less lb active ingredient per acre. In soil samples taken prior to each application and six months after the second application in 2020, significant decreases in *Phytophthora* propagules were found in the treated plots versus the untreated control (Image 1).

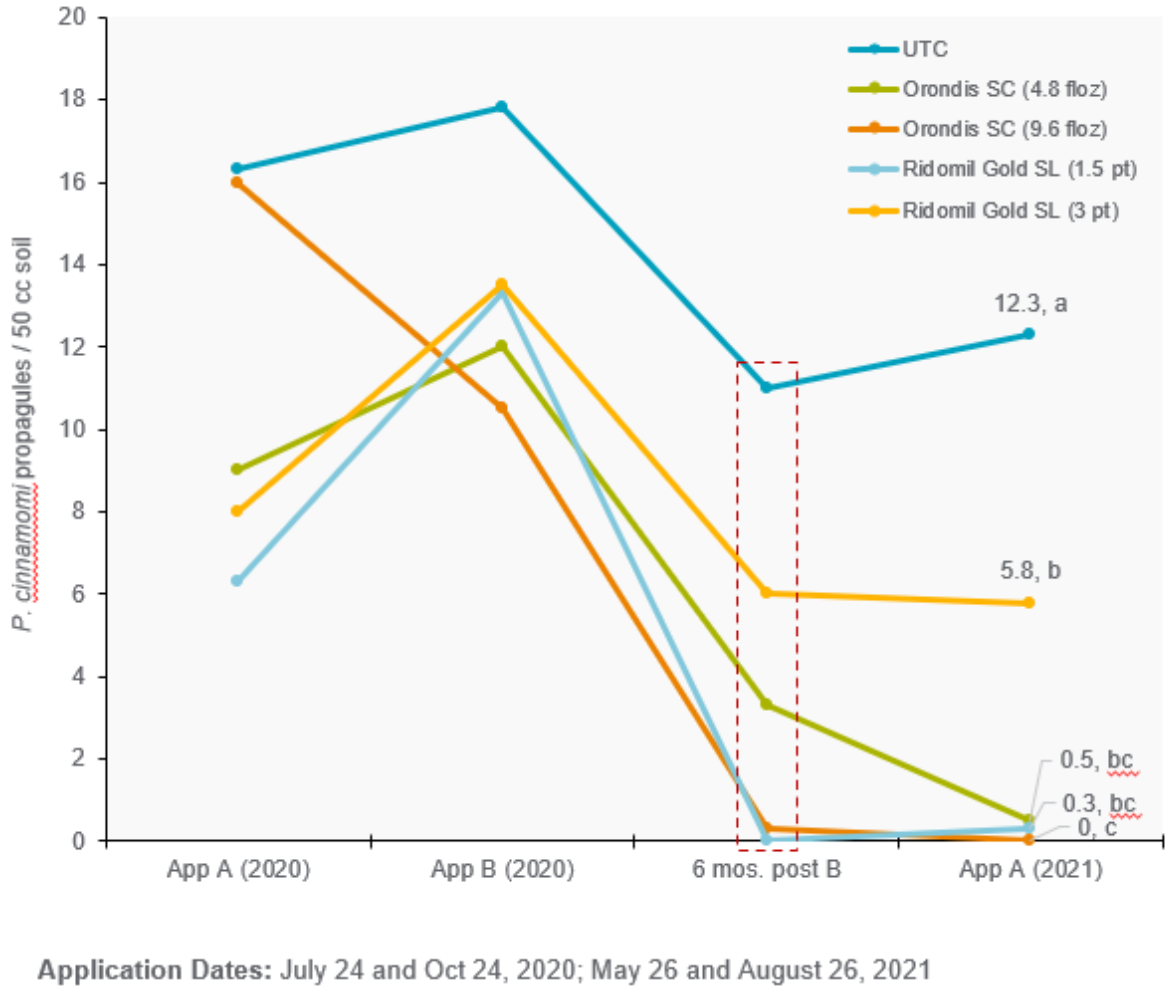

Image 1: *Phytophthora* propagules found in the treated plots versus the untreated control (UTC)

Typically, untreated trees will begin losing leaves earlier in the fall, exhibit a loss of vigor and eventually die due to root loss. In 2020, there was a visual difference seen between the untreated control and both oxathiapiprolin treatments in the fall before harvest (Image 2) and a clear vigor difference at dormancy break in April 2021 (Image 3).

Image 2: Pomegranate trees in the untreated control and both oxathiapiprolin treatments in the fall before harvest.

Image 3: Vigor differences among the untreated control (left) and both oxathiapiprolin treatments at dormancy break in April 2021.

The trees were harvested in September 2021 and all treatments had significantly more fruit than the untreated control (Image 4).

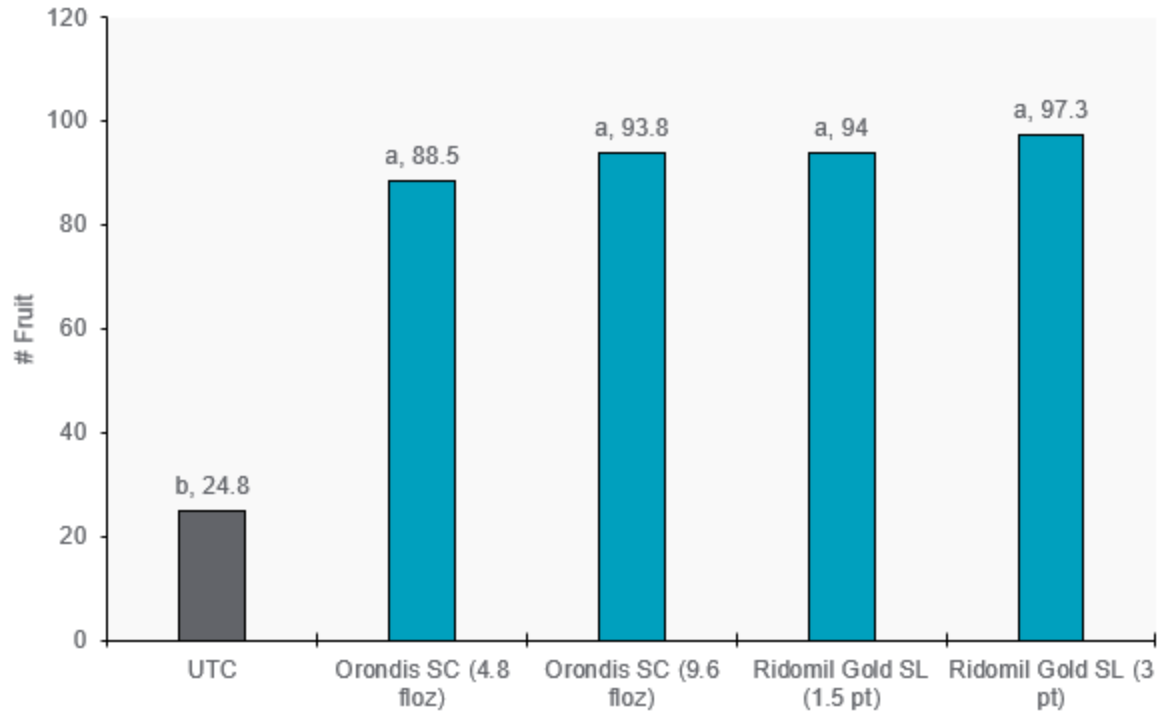

Image 4: Number of fruit harvested from untreated control and pesticide treatments.

Oxathiapiprolin was registered for use on Tropical and Subtropical Fruit (24B) (Nov 2020) and as demonstrated in this case study, is an important tool for growers to control *Phytophthora* on this minor crop.

5.0 REFERENCES

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