Polyoxin D Zinc Salt

Crops

Identification of Petitioned Substance

Chemical Names:
Polyoxin D, Zinc Salt;
Zinc 5-[[2-amino-5-O-(aminocarbonyl)-2-deoxy-L-xylonoyl]-1-(5-carboxy-3,4-dihydro-2,4-dioxo-1(2H)-pyrimidinyl)-1,5-dideoxy-ß-D-allofuranuronate]; b-D-Allofuranuronic acid,5-[[2-amino-5-O-(aminocarbonyl)-2-deoxy-L-xylonoyl]amino]-1-(5-carboxy-3,4-dihydro-2,4-dioxo-1(2H)-pyrimidinyl)-1,5-dideoxy-,zinc salt (1:1) (9CI); Allofuranuronic acid, 5-((2-amino-5-o-(aminocarbonyl)-2-deoxy-L-xylonoyl)amino)-1-(5-carboxy-3,4-dihydro-2,4-dioxo-1(2H)-pyrimidinyl)-1,5-dideoxy-, zinc salt (1:1)

Other Name:
Polyoxirim

Trade Names:
Endorse™; Ph-D™ Water Dispersible Granules; STOPIT™; Veranda™, Veranda-O.

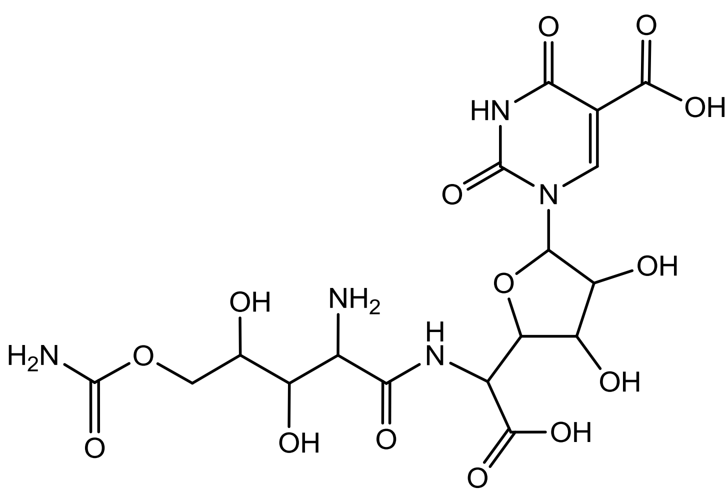
CAS Numbers:
22976-86-9 (polyoxin D)
146659-78-1 (1:1 zinc salt)
33401-46-6 (zinc salt)

Other Codes:
PC 23000

Characterization of Petitioned Substance

<u>Composition of the Substance</u>:
Agricultural antifungal antibiotic complex produced by *Streptomyces cacaoi* var *asoensis* and *S. piomogenus* (O'Neill, 2006). Molecular Formula: $C_{17}H_{23}N_5O_{14} \cdot Zn$ (Chemical Register, 2012). Polyoxins all share a 5-substituted uracil base (Worthington, 1988).

Figure 1
Polyoxin D



Source: ChemBioFinder: 2012
Note: The zinc salt is of the form polyoxin D · Zn

<u>Properties of the Substance</u>:

Table 1
Physical and chemical Properties of Polyoxin D Zinc Salt

Physical or Chemical Property:	Value:
Physical State	Powder
Appearance	Brown
Odor	Musty
Melting Point	122.5 ± 0.2°C; decomposes at 170°C
Solubility	Water: 1.0 g/100 mL
Relative Density at 25°C.	1.864g/cm^3 2.32441 g/cc (20-27.1°C)
pH	7.51 (1% solution, 23.2°C) 6.9 (6.7 - 7.2)

Sources: ChemBioFinder, 2012; LookChem, 2012; Smith, 2012

Specific Uses of the Substance:
Agricultural fungicide; antifungal pharmaceutical.

Approved Legal Uses of the Substance:
EPA Registered.

Action of the Substance:
Inhibits cell wall chitin synthesis (Misato, 1977; O'Neill, 2006).

Combinations of the Substance:
Polyoxin D Zinc Salt pesticides that are used by farmers are formulated with undisclosed inert ingredients. The preferred surfactants used in the dry flowable form are formalin sodium naphthalenesulfonate or non-ionic polyoxyethylene alkyl ethers (Tokumura, et al., 2001). Polyoxin D Zinc Salt may also be mixed with other fungicides.

Status

Historic Use:
Not used in organic production. First isolated in 1966 and reported in 1967 (Bono et al. 1967). First registered for use by EPA 1997. Early registrations were all for turf grass and ornamentals, and toxicity tests were waived (EPA, 2001). EPA first approved food uses in 2008 for the 2009 growing season (Hollis, 2008).

OFPA, USDA Final Rule:
Not listed in the OFPA or USDA NOP Final Rule.

International

Canada - Canadian General Standards Board –
Polyoxin D Zinc Salt does not appear on the CGSB permitted substances List (CGSB, 2011)

CODEX Alimentarius Commission – ftp://ftp.fao.org/docrep/fao/005/Y2772e/Y2772e.pdf
Polyoxin D Zinc Salt does not appear on the Codex Alimentarius Commission's *Guidelines for the Production, Processing, Marketing and Labelling of Organically Produced Foods* Table 2, Substances for Plant Pest and Disease Control (Codex, 2001).

European Economic Community (EEC) Council Regulation, EC No. 834/2007 and 889/2008

The European Union regulation requires all authorized plant protection products to appear on a list of permitted inputs (EC, 2007). Polyoxin D Zinc Salt does not appear on the list of authorized plant protection products and is therefore prohibited (EC, 2008). Other antibiotics used in crop production that are permitted under the NOP are not accepted in the EU Equivalency Agreement (EC, 2012).

International Federation of Organic Agriculture Movements (IFOAM) – Polyoxin D Zinc Salt does not appear on Appendix 2 of the 2005 IFOAM Basic Standards (IFOAM, 2005). No dossier has been received at the time of this report.

Japan Agricultural Standard (JAS) for Organic Production— The Japanese Agricultural Standard for Organic Production does not include polyoxin D Zinc Salt on Table 2, Substances for Plant Pest and Disease Control (JMAFF, 2012).

Evaluation Questions for Substances to be used in Organic Crop or Livestock Production

Evaluation Question #1: What category in OFPA does this substance fall under: (A) Does the substance contain an active ingredient in any of the following categories: copper and sulfur compounds, toxins derived from bacteria; pheromones, soaps, horticultural oils, fish emulsions, treated seed, vitamins and minerals; livestock parasiticides and medicines and production aids including netting, tree wraps and seals, insect traps, sticky barriers, row covers, and equipment cleansers? (B) Is the substance a synthetic inert ingredient that is not classified by the EPA as inerts of toxicological concern (i.e., EPA List 4 inerts) (7 U.S.C. § 6517(c)(1)(B)(ii))? Is the synthetic substance an inert ingredient which is not on EPA List 4, but is exempt from a requirement of a tolerance, per 40 CFR part 180?

Polyoxin D Zinc Salt is a toxin derived from *Streptomyces cacaoi* var. asoensis, a soil-borne microorganism. Other fungicides derived from *Streptomyces* spp. have been considered toxins derived from bacteria consistent with 7 USC 6517(c)(1)(B)(ii)(A) [7 CFR 205.601(i)(10) & (11)].

Evaluation Question #2: Describe the most prevalent processes used to manufacture or formulate the petitioned substance. Further, describe any chemical change that may occur during manufacture or formulation of the petitioned substance when this substance is extracted from naturally occurring plant, animal, or mineral sources (7 U.S.C. § 6502 (21)).

Polyoxin D is produced by controlled fermentation of the naturally occurring soil microorganism *Streptomyces cacaoi* var. asoensis, a soil-borne microorganism. The media used, fermentation conditions and extraction steps were not disclosed in the public version of the petition but are contained in the Confidential Business Information (CBI) version of the petition. The petition states that polyoxin D Zinc Salt is isolated from the broth and dried. Based on the CBI version of the petition, the Zinc Salt appears to be a reaction product and not the naturally occurring form.

The plant pathogen *Alternaria kikuchiana* has developed resistance to various polyoxin fungicides. Manufacturers have used three different approaches to overcome resistance: 1) transnucleosidation; 2) biosynthesis of a polyoxin with the 5-fluorouracil moiety; and 3) decarboxylation of the 5-carboxyuracil polyoxins (Suhadolnik and Reichenbach, 2000).

<u>Evaluation</u> <u>Question #3:</u> Is the substance synthetic? Discuss whether the petitioned substance is formulated or manufactured by a chemical process, or created by naturally occurring biological processes (7 U.S.C. § 6502 (21)).

Based on the information provided in the public version of the petition, it is not possible to determine whether polyoxin D Zinc Salt is synthetic or non-synthetic. The petitioner believes the Zinc Salt of polyoxin D to be non-synthetic. The manufacturing process is contained in the confidential business information (CBI) portion of the petition, and the relevant information was reviewed and considered in development of this report.

A review of all the structural forms of polyoxin does not include the Zinc Salt as a natural product (Worthington, 1988). Naturally occurring polyoxin D is water soluble and has a short residence time on plant surfaces. When used as a pesticide, polyoxin D is formulated as the Zinc Salt to give longer residence time on plant surfaces (EPA, 2008).

The manufacturing process has at least one step that is similar to other *Streptomyces* products that are classified as synthetic on section 205.601 of the National List: streptomycin and tetracycline (terramycin). Similarly, polyoxin D Zinc Salt may also be classified as synthetic.

<u>Evaluation Question #4:</u> Describe the persistence or concentration of the petitioned substance and/or its by-products in the environment (7 U.S.C. § 6518 (m) (2)).

Soil half-life from aerobic microbial metabolism is reported to be 15.9 days. Degradation in water and sunlight is reported to be approximately 2.3 days (Smith, 2012). The petition includes further results of degradation studies under various conditions. Data reviewed by EPA indicated that polyoxin D Zinc Salt biodegrades within 2-3 days of application, with a low toxicity profile [73 FR 69559]. The principal by-products are polyoxin D and uracil-5-carboxylic acid (EPA, 2008). Polyoxin D Zinc Salt degrades very quickly in alkaline soil or in alkaline solutions, and some sources recommend a pH a buffer in the spray tank (Vincelli and Williams, 2012).

<u>Evaluation Question #5:</u> Describe the toxicity and mode of action of the substance and of its breakdown products and any contaminants. Describe the persistence and areas of concentration in the environment of the substance and its breakdown products (7 U.S.C. § 6518 (m) (2)).

Table 2
Toxicity of Polyoxin D Zinc Salt

Toxicological Studies	Toxicity Values	EPA Category
Acute Oral (rats)	LD50>5.0 g/kg	Practically Non-toxic (IV)
Acute Dermal (rats)	LD50>2.0 g/kg	Moderately Toxic (III)
Acute inhalation (rats)	LC50> 4.93 mg/L	IV
Primary eye irritation (rabbits)	N/A	III
Primary dermal irritation (rabbits)	N/A	IV
Dermal sensitization (guinea pigs)	N/A	Not a dermal sensitizer
Chronic Exposure	Negative	No chronic risk
Oncogenicity	Negative	Not an oncogen

Sources: CDPR, 2003; Smith, 2012; US EPA, 2001, 2008.
Signal word CAUTION; N/A- Not applicable.

Polyoxins have long been regarded as antibiotics in both their structure and function (Gottlieb and Shaw, 1970; Worthington, 1988; DeBono and Gordee, 1994; Knight, et al., 1997, Dreikhorn and Owen, 2000;

Suhadolnik and Reichenbach, 2000; EPA, 2001; O'Neill, 2006). Polyoxin D inhibits cell wall chitin synthesis by phytopathogenic fungi (Endo, et al, 1970; Hori, et al., 1971; O'Neill, 2006). Nucleoside antibiotics such as polyoxin D show structural similarities to UDP-N-acetylglucosamine with which they compete for the chitin synthase active site (Dreikhorn and Owen, 2000). Polyoxins are most toxic against the following pathogens: *Alternaria kikuchiana, Pellicularia sasaki, Cochliobolus miyabeanus, Pyricularia oryzae* and *Neurospora crassa* (Hall, 1979).

An increased number of cells with chromosomal aberrations were observed in one study, which could be considered a possible adverse health effect (CDPR, 2003). There has been no follow-up on the CDPR 2003 new active ingredient public report (Leahy, 2012).

<u>Evaluation Question #6:</u> Describe any environmental contamination that could result from the petitioned substance's manufacture, use, misuse, or disposal (7 U.S.C. § 6518 (m) (3)).

The EPA's risk assessment considers polyoxin D Zinc Salt to carry a low environmental risk due to its specific mode of action, low toxicity, rapid degradation and low application rate (EPA, 2008). The EPA waived environmental fate and ground water data due to the use pattern, application methods, and mitigation of non-target aquatic organism toxicity with appropriate precautionary label statements under "Environmental Hazards." Failure to follow the label instructions may result in the death of fish and aquatic organisms (EPA, 2001, 2008).

Biopesticides generally pose substantially lower risks, potentially impact fewer organisms and result in less severe environmental risks than chemically produced synthetic pesticides (EPA, 1999). As a biopesticide and fermentation product, the environmental impact of manufacture is likely considerably less than that for industrially produced pesticides such as copper, sulfur or petroleum distillates. The manufacturing process is biologically based. While the manufacturing process and growth media are CBI, the procedures are similar to the production of other antibiotics produced from *Streptomyces.* Polyoxin D Zinc Salt may be disposed on-site or at an approved waste disposal facility, but should not be disposed of in waste water (Kaken, 2009).

<u>Evaluation Question #7:</u> Describe any known chemical interactions between the petitioned substance and other substances used in organic crop or livestock production or handling. Describe any environmental or human health effects from these chemical interactions (7 U.S.C. § 6518 (m) (1)).

The EPA stated that polyoxin D Zinc Salt was evaluated under the criteria established in the Food Quality Protection Act (FQPA) and the BPPD has not identified any "subchronic, chronic, immune, endocrine or non-dietary cumulative exposure issues that might affect infants and children or the general population" (EPA, 2001, 2008).

As a fungicide used to control soil-borne pathogens, polyoxin D Zinc Salt by definition kills soil fungi. As such, several studies looked at impacts on beneficial fungi introduced in organic farming systems. The effects were found to be mixed. Polyoxin D inhibits the germination of *Trichoderma viride* (Benítez, et al., 1976). *T. viride* is closely related to *T. harzianum*, which is used in organic farming under the brand name Root Shield (OMRI, 2012). *Gliocladium virens, Paecilomyces fumosoroseus* and *Streptomyces griseoviridis* are other fungi used as biological control agents in organic agriculture. *G. virens* is marketed as SoilGard, *P. fumosoroseus* is the active ingredient in PFR-97 and *S. griseoviridis* is sold as Mycostop (OMRI, 2012). Polyoxin D was also found to reduce the efficacy of the virus used to control the black cutwork (*Agrotis ipsilon*) (Bixby-Brosi and Potter, 2012). On the other hand, polyoxin D Zinc Salt promotes the biocontrol of *Bacillus subtilis*, with a strong positive synergistic effect reported for *Alternaria mali* suppression (Yang, et al., 2010).

Evaluation Question #8: Describe any effects of the petitioned substance on biological or chemical interactions in the agro-ecosystem, including physiological effects on soil organisms (including the salt index and solubility of the soil) crops, and livestock (7 U.S.C. § 6518 (m) (5)).

As a broad-spectrum antibiotic and fungicide, polyoxin D Zinc Salt is toxic to soil fungi. Polyoxins and other antibiotics were found to increase melanins in *Alternaria kikuchiana* (Kohno, et al., 1983; Butler and Day, 1998). The ecological functions of melanins are still unknown, but they are believed to enhance the phytotoxic and pathogenic properties of plant pathogens (Butler and Day, 1998). Earthworms were shown to have a preference for melanized fungi (Marfenina and Ischenko, 1997; Butler and Day, 1998).

Beneficial soil organisms may be adversely affected by exposure to polyoxin D. Polyoxin D inhibited the basidiospore germination of wood-decaying fungi (Schmidt, 1987). The nematode-trapping fungus, *Arthrobotrys oligospora*, was less affected by exposure to polyoxin D compared with the plant pathogen *Rhizoctonia solani*, with mixed results. At lower concentrations *A. oligospora* showed abnormalities of growth that resulted in greater trapping at lower concentrations and inhibition of trapping at higher concentrations (Persson and Nordbring-Hertz, 1990). Alternative fungicides such as copper or sulfur may have similar or greater effects on soil ecology, but no studies that compared the impacts of polyoxin D Zinc Salt with commercial fungicides used in organic production were found in the literature. The closest comparison found by the reviewers is a study that examined the use of Nikkomycin Z, another chitin synthesis inhibitor. Nikkomycin Z was found to inhibit hyphal growth and cell wall structures of arbuscular-mycorrhizal fungi (Bago, et al., 1996).

Plant pathogens can acquire resistance to fungicides if exposed to continuous selection by fungicides with a single mode of action (Dekker, 1976). Having additional fungicides with different mode of action to rotate for specific pathogens is a strategy for resistance management. Access to Polyoxin D Zinc Salt by organic farmers may help to impede selection for resistant pathogens, but lack of rotation may result in resistance to fungicides with the same mode of action. Strains of *Alternaria alternata* resistant to Polyoxin B have been isolated in orchards in Japan, where it has been used intensively as a fungicide for many years (Copping and Menn, 2000; Ishii, 2006). Because of their similar structure and mode of action, cross-resistance Extension service specialists report that polyoxin D used on turf is considered to have a moderate risk of resistance (Vincelli and Williams, 2012).

There have been no reported incidents of toxicity to non-target species by any member of the polyoxin family after over 30 years of use (Copping and Duke, 2007). Polyoxin D and other nucleoside antibiotics may be toxic to non-target insects and mites with chitinous cell walls given its mode of action (Hollingworth, 1975). Polyoxin D was shown to inhibit chitin synthetase in cockroaches (Leighton, et al, 1981). It is possible that polyoxin D would have similar activity against other insects with chitinous exoskeletons, some of which are beneficial, such as *Hippodamia convergens,* commonly known as lady beetles (Miyamoto, et al., 1993). However, no adverse effects have been reported against organisms that lack chitinous cell walls (Kim and Hwang, 2007).

Polyoxin D may have a negative effect on the growth of anaerobic rumen fungi when applied to pasture (Cann, et al., 1993).

Evaluation Question #9: Discuss and summarize findings on whether the petitioned substance may be harmful to the environment (7 U.S.C. § 6517 (c) (1) (A) (i) and 7 U.S.C. § 6517 (c) (2) (A) (i)).

Polyoxin D Zinc Salt is moderately toxic to fish and aquatic invertebrates, and should not be discharged into water (Kaken, 2008). Toxicity of technical polyoxin D to wildlife is summarized in Table 3.

Table 3
Technical Polyoxin-D Wildlife Toxicity

Test Animal	Type of Study	Acute Toxicity Value*	Relative Toxicity

Rat (M/F)	Single acute oral dose	>5,000 mg a.i./kg (LD_{50})	Relatively non-toxic
Rainbow trout	Water exposure (96 hrs.)	5.1 mg a.i./l (LC_{50})	Moderately toxic
Daphnia magna	Water exposure (48 hrs.)	1.4 mg a.i./l (LC_{50})	Moderately toxic
Mallard duck	Single acute oral dose	>2,150 mg/kg (LD_{50})	Relatively non-toxic
Mallard duck	Feeding study (8 days)	>5,000 mg/kg (LC_{50})	Relatively non-toxic

* LD_{50}= lethal dose that will kill 50% of test population;
LC_{50}= lethal environmental concentration that will kill 50% of test population.
Source: CDPR, 2003; EPA 2008

The EPA estimated that concentration from runoff of residues into surrounding aquatic habitats from a 10 acre drainage basin into a 6 foot deep 1 acre pond would be approximately 1.6 ppb per 1% residue runoff. Any effects from runoff residues in aquatic environments are expected to be mitigated if the label instructions are followed (EPA, 2001).

Antibiotics released into the environment can lead to the selection of antibiotic resistant organisms, some of which may be plant or human pathogens. Polyoxin D Zinc Salt is a Group 19 fungicide and may result in the selection for resistance of other Group 19 fungicides (Kaken, 2008).

The EPA expects concentrations on foliar surfaces of treated crops to reach maximum residue levels of between 9 ppm and 62 ppm for most plant types. These levels are considered to pose minimal levels of risk to mammalian and avian wildlife based on present toxicological data (EPA, 2001).

Evaluation Question #10: Describe and summarize any reported effects upon human health from use of the petitioned substance (7 U.S.C. § 6517 (c) (1) (A) (i), 7 U.S.C. § 6517 (c) (2) (A) (i)) and 7 U.S.C. § 6518 (m) (4)).

The EPA exempts polyoxin D Zinc Salt from the requirement of a tolerance on almonds, cucurbit vegetables, fruiting vegetables, ginseng, grapes, pome fruits, potatoes, and strawberries [40 CFR 180.1285]. There have been no reported incidents involving polyoxin D poisoning of humans. All polyoxins have been shown to have low mammalian toxicity (Copping and Duke, 2007). Sensitization to skin contact may occur (Kaken, 2011).

Polyoxin D has been shown to be effective as a drug to treat the human and animal pathogens *Candida albicans* and *Cryptococcus neoformans* (Becker, et al., 1983; Hilenski, et al., 1986). Polyoxin D also shows some efficacy in the reduction of the protozoan parasite *Encephalitozoon cuniculi* infecting immune-compromised AIDS patients (Sobottka, et al., 2002).

Evaluation Question #11: Describe all natural (non-synthetic) substances or products which may be used in place of a petitioned substance (7 U.S.C. § 6517 (c) (1) (A) (ii)). Provide a list of allowed substances that may be used in place of the petitioned substance (7 U.S.C. § 6518 (m) (6)).

The naturally occurring quinone plumbagin, isolated as a botanical from the plant *Plumbago capensis* was shown to be equally effective to polyoxin D in the ability to inhibit the incorporation of N-acetylglucosamine into chitin (Dekeyser and Downer, 1994). Plumbagin is not commercially available as a registered pesticide in the US at the present time.

Copper and sulfur both appear on the National List for plant disease control. Various copper and sulfur-based fungicides are allowed for use to control many of the pathogens for which polyoxin D Zinc Salt is labeled. Table 13.a.1 of the petition compares the claimed efficacy of polyoxin D with the claims of other

EPA registered products that have an active ingredient allowed in organic production (Smith, 2012). The petition contains a disclaimer that the table is not comprehensive. In addition to acknowledged omissions, the following errors were noted:

- The labels currently on file for EPA registered products that contain polyoxin D Zinc Salt and mentioned in the petition are not labeled for any use on Brassicas, even though polyoxin D is effective against *Alternaria brassicae* or blackspot (Tewari and Skoropad. 1979).
- Similarly, Endorse WDG, a product that includes polyoxin D Zinc Salt as an active ingredient, does not include uses on many crops for which the alternatives are labeled, including apricots, artichokes, beans, beets, carrots, cherries, celery, chard, citrus, corn, endive, garlic, guava, hops, leeks, lettuce, macadamia, onions, peanuts, peaches, pears, pecans, plums, spinach and walnuts.
- The master label for Endorse WDG does not include shothole for almonds (*Wilsonomyces carpophilus*).
- Similarly, polyoxin D Zinc Salt is not labeled for many fungal and bacterial diseases that the alternative products are legal to use in the US.
- JMS Farms Organic JMS Stylet Oil and Dow's M-Pede Insecticide-Miticide-Fungicide were omitted from the comparisons in the petition.

Table 3 compares the disease control and suppression labels of various alternatives reviewed by OMRI. Formulations that are subregistrations of OMRI listed products and products that make broad claims of suppression without specific crop-pathogen pairs are excluded. The number of options that organic farmers have is greater than Table 3 suggests.

Table 3
Comparison of the Endorse WDG Label with Alternative Pesticides

Crop	Pathogens	EPA Registered and OMRI Listed Products Labeled for Use
Almonds	*Alternaria* spp.	Actinovate SP (Natural Industries); Regalia Concentrate (Marrone); Regalia Maxx (Marrone); Sonata ASO (Agraquest).
Cucurbits (Cucumbers, melons, squash and others)	*Alternaria* spp.	Actinovate SP (Natural Industries); Badge X2 (Isagro); Basic Copper 53 (Albaugh); Champ WG (NuFarm); Chem Copp 50 (apples only) (American Chemet); COC WP (Albaugh); Cueva Fungicide Concentrate (Neudorff); Organic JMS Stylet Oil (JMS); Nordox 75 WG (Nordox); Nu Cop DF (Albaugh); Nu Cop WP (Albaugh); Oxidate (BioSafe); Prestop Biofungicide Powder (Verdura Oy); Regalia Concentrate (Marrone).
	Gray mold (*Botrytis* spp.)	Actinovate SP (Natural Industries); Cueva Fungicide Concentrate (Neudorff).
	Gummy stem blight (*Didymella bryoniae)*	Badge X2 (Isagro); Basic Copper 53 (Albaugh); Chem Copp 50 (apples only) (American Chemet); Champ WG (NuFarm); COC WP (Albaugh); Cueva Fungicide Concentrate (Neudorff); Organic JMS Stylet Oil (JMS); Nordox 75 WG (Nordox); Oxidate (BioSafe); Regalia Concentrate (Marrone); Regalia Maxx (Marrone); Sonata ASO (Agraquest).
	Leaf spot (*Corynespora cassicola*)	Oxidate (BioSafe).
	Powdery mildew (*Spthaerotheca* spp.)	Actinovate SP (Natural Industries); Badge X2 (Isagro); Basic Copper 53 (Albaugh); Champ WG (NuFarm); COC WP (Albaugh); Cosavet DF (Sulphur Mills); CSC 80% Thiosperse (Martin); Cueva Fungicide Concentrate (Neudorff); CSC Dusting Sulfur (Martin); Kaligreen (Otsuka); M-Pede Insecticide-Miticide-Fungicide (Dow); Nordox 75 WG (Nordox); Oxidate (BioSafe); Regalia Concentrate (Marrone); Regalia Maxx (Marrone); Sonata ASO (Agraquest).

Crop	Pathogens	EPA Registered and OMRI Listed Products Labeled for Use
	Scab (*Cladosporium* spp.)	Prestop Biofungicide Powder (Verdura Oy).
Fruit vegetables (Eggplant, pepper, pepinos, tomatillos and tomatoes)	Early blight (*Alternaria solani*)	Actinovate SP (Natural Industries); Badge X2 (Isagro); Basic Copper 53 (Albaugh);); Chem Copp 50 (apples only) (American Chemet); Champ WG (NuFarm); COC WP (Albaugh); Camelot O (SePRO); Cueva Fungicide Concentrate (Neudorff); Organic JMS Stylet Oil (JMS); Nordox 75 WG (Nordox); Nu Cop DF (Albaugh); Nu Cop WP (Albaugh); Oxidate (BioSafe); Prestop Biofungicide Powder (Verdura Oy); Regalia Concentrate (Marrone); Regalia Maxx (Marrone); Sonata ASO (Agraquest).
	Anthracnose (*Colletotrichum coccodes*)	Actinovate SP (Natural Industries); Badge X2 (Isagro); Basic Copper 53 (Albaugh); Champ WG (NuFarm); Chem Copp 50 (apples only) (American Chemet); COC WP (Albaugh); Organic JMS Stylet Oil (JMS); Nordox 75 WG (Nordox); Nu Cop DF (Albaugh); Nu Cop WP (Albaugh); Oxidate (BioSafe).
	Gray molds (*Botrytis* sp.)	Actinovate SP (Natural Industries); Cueva Fungicide Concentrate (Neudorff); Oxidate (BioSafe); Regalia Concentrate (Marrone); Regalia Maxx (Marrone); Sonata ASO (Agraquest).
	Powdery mildew (*Leveillula taurica* and *Oidiopsis sipula*)	Actinovate SP (Natural Industries); Cosavet DF (Sulphur Mills); CSC Dusting Sulfur (Martin); Organic JMS Stylet Oil (JMS); Kaligreen (Otsuka); M-Pede Insecticide-Miticide-Fungicide (Dow); Oxidate (BioSafe); Regalia Concentrate (Marrone); Regalia Maxx (Marrone); Sonata ASO (Agraquest); several other sulfur products by various manufaturers.
Ginseng	*Alternaria panax* spp.	Badge X2 (Isagro); Basic Copper 53 (Albaugh); Champ WG (NuFarm); Cueva Fungicide Concentrate (Neudorff); Nordox 75 WG (Nordox); Nu Cop DF (Albaugh); Nu Cop WP (Albaugh); Oxidate (BioSafe); Regalia Concentrate (Marrone); Regalia Maxx (Marrone); Sonata ASO (Agraquest).
	Botrytis cinerea	Cueva Fungicide Concentrate (Neudorff); Regalia Concentrate (Marrone); Regalia Maxx (Marrone).
	Cylinderocarpon destructans	None found.
	Rhizoctonia solani	Oxidate (BioSafe); Prestop Biofungicide Powder (Verdura Oy); Regalia Concentrate (Marrone).
Grapes	Bunch rot or Gray mold (*Botrytis cinerea)*	CSC Copper Sulfur Dust (Martin); Cueva Fungicide Concentrate (Neudorff); Cueva Fungicide RTU (Neudorff); Organic JMS Stylet Oil (JMS); Oxidate (BioSafe); Regalia Concentrate (Marrone); Regalia Maxx (Marrone).
	Powdery mildew (*Unicula necator*)	Badge X2 (Isagro); Basic Copper 53 (Albaugh); Champ WG (NuFarm); Copper Sulfate Crystals (Chem One); Chem Copp 50 (American Chemet); COC WP (Albaugh); Cosavet DF (Sulphur Mills); CSC 80% Thiosperse (Martin); CSC Copper Sulfur Dust (Martin); CSC Dusting Sulfur (Martin); Cueva Fungicide Concentrate (Neudorff); Cueva Fungicide RTU (Neudorff); Kaligreen (Otsuka); Organic JMS Stylet Oil (JMS); Quimag Quimicos Aguila Copper Sulfate Crystal (Fabrica de Sulfato El Aguila, S.A. de C.V.); Quimag Quimicos Aguila Copper Sulfate Crystal - Crop (Fabrica de Sulfato El Aguila, S.A. de C.V.); Nordox 75 WG (Nordox); Nordox 30/30 WG (Nordox); Nu Cop DF (Albaugh); Nu Cop WP (Albaugh); Oxidate (BioSafe); Regalia Concentrate (Marrone); Regalia Maxx (Marrone); Most OMRI Listed sulfur products.

Crop	Pathogens	EPA Registered and OMRI Listed Products Labeled for Use
Pistachios	*Alternaria* spp.	Badge X2 (Isagro); Basic Copper 53 (Albaugh); COC WP (Albaugh); Nordox 75 WG (Nordox); Nordox 30/30 WG (Nordox); Nu Cop DF (Albaugh); Nu Cop WP (Albaugh); Regalia Concentrate (Marrone); Regalia Maxx (Marrone); Sonata ASO (Agraquest).
	Botryosphaeria spp.	Badge X2 (Isagro); Basic Copper 53 (Albaugh); COC WP (Albaugh); Nordox 75 WG (Nordox); Nordox 30/30 WG (Nordox); Nu Cop DF (Albaugh); Nu Cop WP (Albaugh); Regalia Concentrate (Marrone); Regalia Maxx (Marrone); Sonata ASO (Agraquest).
Pome fruit	Alternaria blotch (*Alternaria mali*)	Regalia Concentrate (Marrone).
	Leaf blotch (*Diplocarpon mali*)	None found.
	Powdery mildew (*Podosphaera leucotricha* in apples; *Phyllactinia mali* in pears)	Golden Micronized Sulfur (Wilbur-Ellis); Organic JMS Stylet Oil (JMS); Kaligreen (Otsuka); Regalia Concentrate (Marrone); Regalia Maxx (Marrone).
	Scab (*Venturia* spp.)	Badge X2 (Isagro); Basic Copper 53 (Albaugh); Blue Shield DF[a] (Albaugh); Camelot O (SePRO); Chem Copp 50[a] (American Chemet); CSC 80% Thiosperse (Martin); Nordox 75 WG (Nordox); Nordox 30/30 WG[a] (Nordox); Oxidate (BioSafe); Regalia Concentrate (Marrone); Regalia Maxx (Marrone).
Potatoes	Early blight (*Alternaria solani*)	Basic Copper 53 (Albaugh); Blue Shield DF (Albaugh); Chem Copp 50 (American Chemet); Champ WG (NuFarm); COC WP (Albaugh); Cueva Fungicide Concentrate (Neudorff); Nordox 75 WG (Nordox); Nu Cop DF (Albaugh); Nu Cop WP (Albaugh); Oxidate (BioSafe); Prestop Biofungicide Powder (Verdura Oy); Regalia Maxx (Marrone); Sonata ASO (Agraquest).
Strawberries	Anthracnose (*Colletotrichum* spp.)	Cueva Fungicide Concentrate (Neudorff); Regalia Concentrate (Marrone); Regalia Maxx (Marrone).
	Gray mold (*Botrytis cinerea*)	Cueva Fungicide Concentrate (Neudorff); Organic JMS Stylet Oil (JMS); Regalia Concentrate (Marrone); Regalia Maxx (Marrone).
	Powdery mildew (*Spthaerotheca*)	Cosavet DF (Sulphur Mills); CSC Dusting Sulfur (Martin); Cueva Fungicide Concentrate (Neudorff); Golden Micronized Sulfur (Wilbur-Ellis); Kaligreen (Otsuka); M-Pede Insecticide-Miticide-Fungicide (Dow); Organic JMS Stylet Oil (JMS); Regalia Concentrate (Marrone); Regalia Maxx (Marrone); several other sulfur products by various manufacturers.

[a] Apples only

Sources: EPA PPLS, 2012; OMRI, 2012.

Information regarding on-farm use of the above-mentioned alternatives should be available from accredited certification agents and access to organic system plans. The reviewers found only a limited number of studies that compare efficacy of polyoxin D Zinc Salt with pesticides that are currently approved for organic production.

The only two crop-disease pairs for which there were no pesticidal alternatives approved for organic production are *C. destructans* root rot in ginseng and *Diplocarpon mali* leaf blotch in apples. Researchers showed that the biological control agent *Gliocladium catenulatem* applied as the OMRI Listed product Prestop controlled *C. destructans* in ginseng comparable to the chemical fungicide metalaxyl-M (Rahman and Punja, 2007). Prestop is not currently labeled for *C. destructans* on ginseng. Blotches caused by *Alternaria mali* and *Diplocarpon mali* are not identified as a serious problem in US organic apple production (Swezey, 2000; Craver, et al., 2008; Delate, et al., 2008; Peck and Merwin, 2009). In California, the only labeled are for turf, grass, pistachios and grapes (Arysta, 2010, 2011; Leahy, 2012).

__Evaluation Question #12:__ Describe any alternative practices that would make the use of the petitioned substance unnecessary (7 U.S.C. § 6518 (m) (6)).

NOP Standards require that a producer must use certain specific management practices. Among the management practices required are crop rotations, crop nutrient management practices, sanitation to remove disease vectors, and the selection of resistant species and varieties [7 CFR 205.206(a)]. In addition, before any fungicide that appears on the National List can be used, a producer must also document that disease suppressive practices as well as non-synthetic biological, botanical or mineral inputs are insufficient to prevent, suppress or control diseases [7 CFR 205.206(d) & (e)].

Antibiosis as a mode of action for plant disease suppression in soils is a relatively new approach. The use of live organisms rather than their extracts offers a more ecological approach to manage plant pathogens and is seen as more consistent with organic farming principles (Milner, et al., 1997). Beneficial antagonistic *Streptomyces* spp. may be promising biological control agents (Liu, et al., 1997), but development and commercialization has been slow.

Improved monitoring techniques can help ginseng growers avoid planting into soils that are infested with *Cylinderocarpon descructans* (Kernaghan et al., 2007). Rotations with brassicas, such as mustard cover crops, can biofumigate soils and suppress *C. destructans* when an infestation has occurred (Crosby, et al., 2010).

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