

Formal Recommendation
From: National Organic Standards Board (NOSB)
To: the National Organic Program (NOP)

Date:

Subject:

Chair:

The NOSB hereby recommends to the NOP the following:

Rulemaking Action:

Guidance Statement:

Other:

Statement of Recommendation: (Motion # 1)

Motion to classify Polyoxin D Zinc Salt as petitioned as synthetic.

Rationale Supporting Recommendation (including consistency with OFPA and NOP):

Source of zinc used in formulation possibly from a synthetic source. Petitioner could not be sure. The manufacturer has chosen to withhold disclosure of its manufacturing process, citing it as proprietary and confidential business information. As stated in the 2012 technical review (TR), which was based on the un-redacted version of the petition, the Zinc Salt appears to be a reaction product and not a naturally occurring form. The TR also states that the manufacturing process has at least one step that would be similar to other *Streptomyces* products that are classified as synthetic on section 205.601 of the National List: streptomycin and tetracycline (terramycin).

Committee Vote:

Moved:

Seconded:

Yes:

No:

Abstain:

Absent:

Recuse:

Statement of Recommendation: (Motion # 2)

Failed

To add Polyoxin D Zinc Salt to the National List at 205.601 as a Synthetic Substance Allowed for Use in Organic Production.

Rationale Supporting Recommendation (including consistency with OFPA and NOP):

This material was deemed non-essential. Furthermore, it presented environmental concerns for soil bacteria and fungi health because it was a broad spectrum fungicide.

Committee Vote:

Moved: Colehour Bondera

Seconded: John Foster

Yes: 6

No: 9

Abstain: 0

Absent: 0

Recuse: 0

**National Organic Standards Board
Crops Subcommittee
Petitioned Material Proposal
Polyoxin D Zinc Salt**

January 29, 2013

Polyoxin D Zinc Salt was petitioned in 2012 as a Synthetic Substance to be Allowed for Use in Organic Crop Production (7CFR 205.601).

Polyoxin D Zinc Salt (EPA Reg. No. 68173-1) is a fungicide derived from *Streptomyces cacaoi* var. *asoensis*, a soil-borne microorganism, through an aerobic fermentation process. While it appears that the polyoxin D may be a naturally derived material, the added zinc salt may or may not be synthetic. The manufacturer of Polyoxin D Zinc Salt could not confirm the source of the Zinc Salt, as to whether it was “virgin” zinc from a mine or from a recycled zinc source. Thus, it would have to be considered a synthetic material. The zinc salt is added to give the polyoxin D a longer residual time on the plant surface. The manufacturer has chosen to withhold disclosure of its manufacturing process, citing it as proprietary and confidential business information. As stated in the 2012 technical review (TR), which was based on the un-redacted version of the petition, the Zinc Salt appears to be a reaction product and not a naturally occurring form.

The petitioner has submitted several petition amendments that include an expanded tolerance exemption for polyoxin D zinc salt from EPA for use on all food commodities and expanded use allowances for all food and feed crops. This includes both pre-harvest and post-harvest uses. Some examples of plant diseases and pathogens for which its use is intended to control are: Alternaria, Anthracnose, Botrytis, Brown Patch, Downy Mildew, Powdery Mildew, and Rhizoctonia.

Polyoxin D zinc salt is a fungicide labeled for use on an expanded list of crops. It works as a fungistatic material, rather than with fungicidal activity. This means that rather than killing the bacteria or fungi, it inhibits the growth of the fungi colony by inhibiting the chitin growth in the cell walls. Polyoxin D zinc salt is used exclusively on plants. It is not registered for use as an antibiotic in human or veterinary medicine. However, the TR indicates that polyoxin D zinc is a broad spectrum fungicide, raising concerns about its impact on beneficial soil organisms, citing its residual life in soil. While it has impact on non-target beneficial fungi and bacteria in the soil, proponents of this material maintain that it should not have a long lasting effect due to its mode of action and short half-life in water. While there are concerns raised about the effect on beneficial fungi and insects, supplemental data submitted by the petitioner attempts to address the majority of these concerns on an individual basis.

The EPA lists polyoxin D zinc salt (EPA Reg. No. 68173-1) as a Fungicide Resistance Action Committee (FRAC) Code of 19 i.e., the target site of action is a chitin synthetase. This means that it has a unique mode of action, which proponents of its use cite as extremely useful in a rotational fungicide program in organic farming operations as a resistance management tool. The TR listed a number of alternative materials and practices. The majority of the Subcommittee members found this to be incompatible with organic practices.

Evaluation Criteria

(Applicability noted for each category; Documentation attached)

Criteria

Satisfied?

- 1. Impact on Humans and Environment Yes No
 - N/A
 - a. Essential & Availability Criteria Yes No
 - N/A
- 2. Compatibility & Consistency Yes No
 - N/A
- 3. Commercial Supply is Fragile or Potentially Unavailable Yes No
 - N/A
 - as Organic (only for § 205.606)

Substance Fails Criteria Category: [2, 3] Comments:

Proposed Annotation (if any):

Basis for annotation: To meet criteria above Other regulatory criteria

Citation

Notes:

Recommended Committee Action & Vote, including classification recommendation (state actual motion):

Classification Motion: Motion to classify Polyoxin D Zinc as petitioned as synthetic.

Motion by: Harold Austin

Seconded by: Colehour Bondera

Yes: 8 No: 0 Absent: 0 Abstain: 0 Recuse: 0

Listing Motion: To add Polyoxin D Zinc Salt to the National List at § 205.601 as a Synthetic Substance Allowed for Use in Organic Crop Production.

Motion by: Harold Austin

Seconded by: Colehour Bondera

Yes: 3 No: 4 Absent: 0 Abstain: 1 Recuse: 0

Crops	<input checked="" type="checkbox"/>	Agricultural	<input type="checkbox"/>	Allowed¹	<input type="checkbox"/>
Livestock	<input type="checkbox"/>	Non-synthetic	<input type="checkbox"/>	Prohibited²	<input type="checkbox"/>
Handling	<input type="checkbox"/>	Synthetic	<input checked="" type="checkbox"/>	Rejected³	<input checked="" type="checkbox"/>
No restriction	<input type="checkbox"/>	Commercial unavailable as organic	<input type="checkbox"/>	Deferred⁴	<input type="checkbox"/>

¹Substance voted to be added as “allowed” on National List to § 205. with Annotation (if any):

²Substance to be added as “prohibited” on National List to § 205. with Annotation (if any):

Describe why a prohibited substance:

³Substance was rejected by vote for amending National List to § 205. . Describe why material was rejected:

⁴Substance was recommended to be deferred because
If follow-up needed, who will follow up:

Approved by Subcommittee Chair to Transmit to NOSB

Jay Feldman, Subcommittee Chair

January 29, 2013

NOSB Evaluation Criteria for Substances Added To the National List

Category 1. Adverse impacts on humans or the environment? Substance:

Question	Yes	No	N/A ¹	Documentation (TAP; petition; regulatory agency; other)
1. Are there adverse effects on environment from manufacture, use, or disposal? [§205.600 b.2]			X	
2. Is there environmental contamination during manufacture, use, misuse, or disposal? [§6518 m.3]	X			The TR (lines 190-195) states that the EPA considers polyoxin D zinc salt a low environmental risk, listing several reasons for this rationale. Also, included in the supplemental information submitted by the petitioner on October 2, 2012 as part of an EPA posting to the Federal Register on September 12, 2012. The TR does mention (line 194) that failure to follow the product label could result in death of fish and aquatic organisms. In the TR (lines 197-204) states that biopesticides generally pose lower risks than chemically produced pesticides. The manufacturing process is CBI, but the TR states the process would be similar to other antibiotics produced from <i>Streptomyces</i> . (TR July 11, 2102) The TR states (lines 190-204) that polyoxin D could get into water if misused by not following the label. Waste may be disposed of on site or at an approved waste facility, but not disposed of in waste water. (TR July 11, 2012)
3. Is the substance harmful to the environment and biodiversity? [§6517c(1)(A)(i);6517(c)(2)(A)i]	X	X		Polyoxin D zinc salt is moderately toxic to fish and aquatic invertebrates and should not be discharged into water. (TR lines 279-280). If label instructions followed, those concerns would be mitigated (EPA,

				2001)(TR lines 290-291). Should be considered toxic to various soil fungi and bacteria (TR lines 234-235). However, the TR (lines241-251) does state that alternative fungicides, such as copper or sulfur, may have similar or more severe effects. No documented studies to verify the effects by comparison to other fungicides. In the TR it mentions (TR line 54) Action of Substance: Inhibits cell wall chitin synthesis (Misato, 1977, O'Neill, 2006). It further states (TR lines 257-262) it has been shown to inhibit chitin synthetase in cockroaches, and may therefore affect beneficial insects. EPA: Toxic to Honey Bees. ¹ Kaken cites EPA ² Polyoxin D and its zinc salt do not inhibit the synthesis of chitin in animals that contain chitin, such as for insects and crustaceans that contain chitin in their exoskeletons.
4. Does the substance contain List 1, 2 or 3 inerts? [§6517 c (1)(B)(ii); 205.601(m)2]		?		The TR states that Polyoxin D Zinc Salt is formulated with undisclosed inert ingredients. TR line 58 (TR July 11, 2012) The TR further states that the preferred surfactants used in the dry flowable form are formalin sodium naphthalenesulfonate (inert list 4B) or non-ionic polyoxyethylene alkyl ethers (inert list 4B) (Tokumura, et al., 2001). Formulation process is CBI
5. Is there potential for detrimental chemical interaction with other materials used? [§6518 m.1]	X	X		Because of its activity as a fungicide, it may have a negative impact on beneficial fungi. Polyoxin D inhibits the germination of <i>Trichoderma viride</i> (Benitez, et al., 1976). <i>T. viride</i> is closely related to <i>T.harzianum</i> , which is used in organic farming under the brand name Root Shield (OMRI, 2012). There are a couple of other fungi used as biological controls in organic farming. (TR lines216-222). However, it has also been shown to promote the biocontrol of <i>Bacillus subtilis</i> , with a strong synergistic effect on <i>Alternaria mali</i> suppression. (TR lines 225-226) (TR July 11, 2012) Also, in the TR (TR lines 220-224) it lists <i>Gliocladium virens</i> , <i>Paecilomyces fumosoroseus</i> , and <i>Streptomyces griseoviridis</i> as other fungi used as biological control agents in organic

¹ EPA, May 11 ,2012, Science Review of Product Chemistry, Residue Chemistry, Non-Target Organism, and Toxicity Data in Support of Label Amendment for Polyoxin D Zinc Salt. (Included with supplemental petition)

² EPA, May 11 ,2012, Science Review of Product Chemistry, Residue Chemistry, Non-Target Organism, and Toxicity Data in Support of Label Amendment for Polyoxin D Zinc Salt. (Included with supplemental petition).

			<p>agriculture. <i>G virens</i> is marketed as SoilGard, <i>P. fumosoroseus</i> is the active ingredient in PFR-97 and <i>S.griseoviridis</i> is sold as Mycostop (OMRI, 2012). (TR line 223) states that polyoxin D zinc salt was found to reduce the efficacy of the virus used to control the black cutwork (sic)(<i>Agrotis ipsilon</i>) (Bixby-Brosi and Potter, 2012 In the soil tests, the half-lives were 15.9 days for aerobic soils and 59.2 days for anaerobic soils. (EPA science review, p12). However, in the document provided by the petitioner (January 18,2013 section 5.2) it states that in the presence of sunlight polyoxin D zinc salt degrades by 50% within 0.4 days (9.6 hours) “in sterile natural water, pH 5.0, pH 7.0, and pH 9.0 buffers, respectively.” The petitioner says that it inhibits fungi growth but does not kill it, maintain that it would not be a detriment to organic products such as Root Shield, currently used in organic farming (same doc. Pg 24 section 5.5).</p>
<p>6. Are there adverse biological and chemical interactions in agro-ecosystem? [§6518 m.5]</p>	<p>X</p>	<p>X</p>	<p>TR 233-237: “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 <i>Alternaria kikuchiana</i> (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).” There is some concern that polyoxin D used on turf to have a moderate risk of resistance. (Vincelli and Williams 2012)(TR lines 253-261) Again alternative materials may have similar or worse effects.(TR lines 246-248) (TR July 11, 2012) In the Jan. 18, 2013 (pages 20 -26) document provided by the petitioner it does not actually kill fungi, just inhibits growth. Also is not harmful to beneficial insects. Same report (pages 27-28) also that polyoxin D zinc salt is a FRAC 19 class (Kaken 2008) (EPA Reg. No. 68173-1) of fungicide. It has a unique mode of action that would aid in resistance management</p>

				as part of an IPM disease control program. Only class 19 fungicide currently listed.
7. Are there detrimental physiological effects on soil organisms, crops, or livestock? [§6518 m.5]	X			The TR states that there may be adverse effects to beneficial soil organisms when exposed to polyoxin D. TR lines 241-242. It goes on to state that alternative fungicides may have similar or even greater effects on soil ecology, but that no studies could be found that compare the impacts between polyoxin D and other fungicides in organic production, specifically. TR lines 246-251. (TR July 11, 2012) Is not labeled for use on livestock or pastures.
8. Is there a toxic or other adverse action of the material or its breakdown products? [§6518 m.2]		X		The following refers to polyoxin D zinc's use as an antibiotic: Polyoxin D has been shown to be effective as a drug to treat human and animal pathogens <i>Candida albicans</i> and <i>Cryptococcus neoformans</i> (Becker, et al., 1983; Hilenski, et al., 1986). Polyoxin D also shows some efficacy in the reduction of the protozoan parasite <i>Encephalitozoon cuniculi</i> infecting immune-compromised AIDS patients (Sobottka, et al., 2002). All three of the above mentioned studies were <i>in vitro</i> experiments and not substantiated by any <i>in vivo</i> claims or studies. Polyoxin D zinc salt in currently not listed for use in human or veterinary medicine. Moderate acute dermal toxicity; moderate toxicity primary eye irritation. (TR Table 2.)
9. Is there undesirable persistence or concentration of the material or breakdown products in environment? [§6518 m.2]		X		The EPA's risk assessment of 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) TR lines 190-191. "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 194 aquatic organisms (EPA, 2001, 2008)." (TR 191-195) 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). (TR line 153)(July 11, 2012)
10. Is there any harmful	X	X		All polyoxins have shown to have low

<p>effect on human health? [§6517 c (1)(A)(i); 6517 c(2)(A)i; §6518 m.4]</p>				<p>mammalian toxicity.(Copping and Duke, 2007)(TR lines 305-309)). Could cause slight skin irritation. Positive benefits for human and animal pathogens <i>Candida albicans</i> and <i>Cryptococcus neoformans</i> (Becker, et al. 1983; Hilenski, et al., 1986) (TR lines 311-314) Polyoxin D Zinc Salt is currently not listed for use for human or veterinary medicinal uses. Also has been shown to have an effect on the protozoan parasite <i>Encephalitozoon cuniculi</i> infecting the immune system in AIDS patients (Sobottka, et al., 2002) (TR lines 311-314) This was the result of one <i>in vitro</i> experiment. (TR July 11,2012) EPA: results of the mutagenicity studies indicated Polyoxin D Zinc Salt Technical was weakly mutagenic in an Ames Assay (MRID# 433230-01) and not mutagenic in a host mediated assay (MRID # 432618-36). If a food/feed use is ever sought, the test results will require a review of the mutagenicity data base to determine the need for additional studies.²Mammalian chromosome aberration studies with hamster cells showed highly significant increases in chromosomal aberrations over solvent control.³ However, in view of other studies submitted by the petitioner, EPA decided that the studies indicate that polyoxin D zinc salt is not mutagenic or clastogenic.</p>
<p>11. Is there an adverse effect on human health as defined by applicable Federal regulations? [205.600 b.3]</p>			X	
<p>12. Is the substance GRAS when used according to FDA's good manufacturing practices? [§205.600 b.5]</p>			X	
<p>13. Does the substance contain residues of heavy metals or other contaminants in excess of FDA tolerances? [§205.600 b.5]</p>			X	

¹If the substance under review is for crops or livestock production, all of the questions from 205.600 (b) are N/A—not applicable.

² EPA. Consideration of Eligibility for Registration of the New Pesticide Active Ingredient Polyoxin D Zinc Salt – DECISION MEMORANDUM,p 15.

³ EPA, May 11, 2012. Science Review of Product Chemistry, Residue Chemistry, Non-Target Organism, and Toxicity Data in Support of Label Amendment for Polyoxin D Zinc Salt. (Included with supplemental petition.)

NOSB Evaluation Criteria for Substances Added To the National List

Category 2. Is the Substance Essential for Organic Production? Substance:

Question	Yes	No	N/A ¹	Documentation (TAP; petition; regulatory agency; other)
1. Is the substance formulated or manufactured by a chemical process? [6502 (21)]	X	X		Included in a new document received on January 18, 2013 from the petitioner it states on page 5 section 1.1, that, polyoxin D is made from an aerobic fermentation process, thus a natural process. However, they do state that they do not know whether the zinc salt is from a mined or from a recycled zinc source. The TR states that the manufacturing process has at least one step that would be similar to other <i>Streptomyces</i> 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 a synthetic. TR lines 146-148. It would appear that polyoxin D may be non-synthetic, but it would be assumed that the zinc salt would be synthetic, due to the lack of being able to properly verify its source.
2. Is the substance formulated or manufactured by a process that chemically changes a substance extracted from naturally occurring plant, animal, or mineral, sources? [6502 (21)]	X	X		Refer to the above answer in Category 2, Question 1.
3. Is the substance created by naturally occurring biological processes? [6502 (21)]		X		It is produced from a natural occurring soil microorganism <i>Streptomyces cacaoi</i> by a controlled fermentation process, according to the TR lines 119 – 120. (TR July 11, 21012) The petition states that polyoxin D Zinc Salt is isolated from a broth (extraction media) and then dried.

				Actual process is part of their CBI information. One part of the TR states that a review of all the structural forms of polyoxin does not include the Zinc Salt as a natural product (Worthington, 1988). TR lines 141-142. Also, refer to the answers as stated in Category 2, Question 1 & 2.
4. Is there a natural source of the substance? [§205.600 b.1]		X	X	
5. Is there an organic substitute? [§205.600 b.1]			X	
6. Is the substance essential for handling of organically produced agricultural products? [§205.600 b.6]			X	
7. Is there a wholly natural substitute product? [§6517 c (1)(A)(ii)]	X	X		There is a natural occurring quinone plumbagin, isolated as a botanical that is comparable to polyoxin D (Dekeyser and Downer 1994), but it is not commercially available in the US at this time. There are coppers and sulfur materials currently allowed for use. TR 321-328. (TR July 11, 2012)
8. Is the substance used in handling, not synthetic, but not organically produced? [§6517 c (1)(B)(iii)]			X	
9. Are there any alternative substances? [§6518 m.6]	X			There are other alternative substances available. The TR lists several that are currently allowed: JMS Stylet Oil, Dow's M-Pede, Regalia, Sonata, and Kaligreen to name just a few. See TR July 12, 2012 table: Comparison of the Endorse WDG label with Alternative Pesticides., located between lines 355-356. The efficacy of each of these materials is not listed.
10. Is there another practice that would make the substance unnecessary? [§6518 m.6]	X	X		(TR lines 376-391) The TR lists several possible practices that could be used possibly in place of polyoxin D Zinc Salt. Antibiosis – using the live organisms rather than their extracts. This seems to be more consistent with organic farming principles.(Milner, et al. 1997) Also beneficial antagonistic Streptomyces spp – but commercial development is slow in coming.(Liu, et al., 1997) (TR July 11, 2012) Also, crop rotation, crop nutrient management practices,

				sanitation to remove disease vectors, selection of resistant species and varieties (where applicable) beneficial antagonistic bacteria, monitoring. TR 367-382
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¹If the substance under review is for crops or livestock production, all of the questions from 205.600 (b) are N/A—not applicable.

NOSB Evaluation Criteria for Substances Added To the National List

Category 3. Is the substance compatible with organic production practices?

Substance:

Question	Yes	No	N/A ¹	Documentation (TAP; petition; regulatory agency; other)
1. Is the substance compatible with organic handling? [§205.600 b.2]			X	
2. Is the substance consistent with organic farming and handling? [§6517 c (1)(A)(iii); 6517 c (2)(A)(ii)]	X	X		There are concerns with the possible impact on beneficial soil organisms. Toxic to bees. (TR lines 305-309) EPA exempts it from tolerance (40 CFR 180.1285) Also in a petition Addendum dated October 2,2012 the EPA has granted the petitioner an expanded exemption of tolerance to “all food commodities” and given expanded uses for all food and feed crops pre-harvest and post- harvest.
3. Is the substance compatible with a system of sustainable agriculture? [§6518 m.7]	X	X		No, because it is not a unnecessary synthetic input. Also, because it does show toxicity to fungi and bees. However, some felt it was a useful tool as part of a rotational disease control program.
4. Is the nutritional quality of the food maintained with the substance? [§205.600 b.3]			X	
5. Is the primary use as a preservative? [§205.600 b.4]			X	
6. Is the primary use to recreate or improve flavors, colors, textures, or nutritive values lost in processing (except when required by law, e.g., vitamin D in milk)? [205.600 b.4]			X	
7. Is the substance used in production, and does it contain an active synthetic ingredient in the following		X		

categories:				
a. copper and sulfur compounds;				
b. toxins derived from bacteria;	X			According to the TR (TR line 110) polyoxin D is a toxin derived from a bacteria (<i>Streptomyces cacaoi</i> var. <i>asoensis</i>) (TR July 11, 2012)
c. pheromones, soaps, horticultural oils, fish emulsions, treated seed, vitamins and minerals?		X		
d. livestock parasiticides and medicines?		X		
e. production aids including netting, tree wraps and seals, insect traps, sticky barriers, row covers, and equipment cleaners?		X		

¹If the substance under review is for crops or livestock production, all of the questions from 205.600 (b) are N/A—not applicable.

NOSB Evaluation Criteria for Substances Added To the National List

Category 4. Is the commercial supply of an agricultural substance as organic, fragile or potentially unavailable? [§6610, 6518, 6519, 205.2, 205.105 (d), 205.600 (c) 205.2, 205.105 (d), 205.600 (c)] **Substance: Name**

Question	Yes	No	N/A ¹	Documentation (TAP; petition; regulatory agency; other)
1. <u>Is the comparative description provided</u> as to why the non-organic form of the material /substance is necessary for use in organic handling?			X	
2. Does the current and historical industry information, research, or evidence provided explain how or why the material /substance cannot be obtained organically in the appropriate form to fulfill an essential function in a system of organic handling?			X	
3. Does the current and historical industry information, research, or evidence provided explain how or why the material /substance cannot be obtained organically in the appropriate quality to fulfill an essential function in a system of organic handling?			X	

4. Does the current and historical industry information, research, or evidence provided explain how or why the material /substance cannot be obtained organically in the appropriate quantity to fulfill an essential function in a system of organic handling?			X	
5. Does the industry information provided on material / substance non-availability as organic, include (but not limited to) the following: a. Regions of production (including factors such as climate and number of regions);			X	
b. Number of suppliers and amount produced;			X	
c. Current and historical supplies related to weather events such as hurricanes, floods, and droughts that may temporarily halt production or destroy crops or supplies;			X	
d. Trade-related issues such as evidence of hoarding, war, trade barriers, or civil unrest that may temporarily restrict supplies; or			X	
e. Are there other issues which may present a challenge to a consistent supply?			X	

¹If the substance under review is for crops or livestock production, all of the questions from 205.600 (b) are N/A—not applicable.