Petition to Amend 7 CFR §205.601 to Add Polyoxin D Zinc Salt as a Synthetic Substance Allowed for Use In Organic Crop Production: Addendum 1

PUBLIC DOCUMENT

Submitted by
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January 25, 2012
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Published final rule that expands the tolerance exemption for polyoxin D zinc salt to include "all food commodities"

EPA-APPROVED REGULATIONS IN THE WEST VIRGINIA SIP

State citation [Chapter 16–20 or 45 CSR]	Title/subject	State effective date	EPA approval date	Additional explanation/ citation at 40 CFR 52.2565
* * *	*	*	*	* *
[45 CSR] Series 8 Ambient Air Quality Standards				
Section 45–8–1	General	6/16/11	9/12/12 [Insert page number where the document begins].	Incorporation by reference of the National Ambient Air Quality Standards.
Section 45–8–2	Definitions	6/16/11	9/12/12 [Insert page number where the document begins].	Revised section moved from 45–8–3 to 45–8–2.
Section 45–8–3	Adoption of Standards	6/16/11	9/12/12 [Insert page number where the document begins].	Section was revised to read new title and content.
Section 45–8–4	Inconsistency Between Rules	6/16/11	9/12/12 [Insert page number where the document begins].	Revised section moved from 45–8–7 to 45–8–4.
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[FR Doc. 2012–22338 Filed 9–11–12; 8:45 am]

BILLING CODE 6560–50–P

ENVIRONMENTAL PROTECTION AGENCY

40 CFR Part 180

[EPA–HQ–OPP–2011–1028; FRL–9360–6]

RIN 2070

Polyoxin D Zinc Salt; Amendment to an Exemption From the Requirement of a Tolerance

AGENCY: Environmental Protection Agency (EPA).

ACTION: Final rule.

SUMMARY: This regulation amends the existing exemption from the requirement of a tolerance for residues of polyoxin D zinc salt when used as a fungicide on almonds, cucurbit vegetables, fruiting vegetables, ginseng, grapes, pistachios, pome fruits, potatoes, and strawberries by expanding the current exemption to include all food commodities. This regulation establishes an exemption from the requirement of a tolerance for residues of polyoxin D zinc salt in or on all food commodities when applied as a fungicide and used in accordance with good agricultural practices. On behalf of Kaken Pharmaceutical Co., Ltd., Conn & Smith, Inc. submitted a petition to EPA under the Federal Food, Drug, and Cosmetic Act (FFDCA), requesting that EPA amend the existing exemption from the requirement of a tolerance for polyoxin D zinc salt. This regulation eliminates the need to establish a maximum permissible level for residues of polyoxin D zinc salt under the FFDCA.

DATES: This regulation is effective September 12, 2012. Objections and requests for hearings must be received on or before November 13, 2012, and must be filed in accordance with the instructions provided in 40 CFR part 178 (see also Unit I.C. of the **SUPPLEMENTARY INFORMATION**).

ADDRESSES: The docket for this action, identified by docket identification (ID) number EPA–HQ–OPP–2011–1028, is available at http://www.regulations.gov or at the Office of Pesticide Programs Regulatory Public Docket (OPP Docket) in the Environmental Protection Agency Docket Center (EPA/DC), EPA West Bldg., Rm. 3334, 1301 Constitution Ave. NW., Washington, DC 20460–0001. The Public Reading Room is open from 8:30 a.m. to 4:30 p.m., Monday through Friday, excluding legal holidays. The telephone number for the Public Reading Room is (202) 566–1744, and the telephone number for the OPP Docket is (703) 305–5805. Please review the visitor instructions and additional information about the docket available at http://www.epa.gov/dockets .

FOR FURTHER INFORMATION CONTACT: Colin G. Walsh, Biopesticides and Pollution Prevention Division (7511P), Office of Pesticide Programs, Environmental Protection Agency, 1200 Pennsylvania Ave. NW., Washington, DC 20460–0001; telephone number: (703) 308–0298; email address: *walsh.colin@epa.gov*.

SUPPLEMENTARY INFORMATION:

I. General Information

A. Does this action apply to me?

You may be potentially affected by this action if you are an agricultural producer, food manufacturer, or pesticide manufacturer. The following list of North American Industrial Classification System (NAICS) codes is not intended to be exhaustive, but rather provides a guide to help readers determine whether this document applies to them. Potentially affected entities may include:

- Crop production (NAICS code 111).
- Animal production (NAICS code 112).
- Food manufacturing (NAICS code 311).
- Pesticide manufacturing (NAICS code 32532).

B. How can I get electronic access to other related information?

You may access a frequently updated electronic version of 40 CFR part 180 through the Government Printing Office's e-CFR site at *http://ecfr.gpoaccess.gov/cgi/t/text/text-idx?&c=ecfr&tpl=/ecfrbrowse/Title40/40tab_02.tpl*.

To access the OCSPP test guidelines referenced in this document electronically, please go to *http://www.epa.gov/ocspp* and select "Test Methods and Guidelines."

C. How can I file an objection or hearing request?

Under FFDCA section 408(g), 21 U.S.C. 346a, any person may file an objection to any aspect of this regulation and may also request a hearing on those objections. You must file your objection

or request a hearing on this regulation in accordance with the instructions provided in 40 CFR part 178. To ensure proper receipt by EPA, you must identify docket ID number EPA–HQ–OPP–2011–1028 in the subject line on the first page of your submission. All objections and requests for a hearing must be in writing, and must be received by the Hearing Clerk on or before November 13, 2012. Addresses for mail and hand delivery of objections and hearing requests are provided in 40 CFR 178.25(b).

In addition to filing an objection or hearing request with the Hearing Clerk as described in 40 CFR part 178, please submit a copy of the filing (excluding any Confidential Business Information (CBI) for inclusion in the public docket. Information not marked confidential pursuant to 40 CFR part 2 may be disclosed publicly by EPA without prior notice. Submit the non-CBI copy of your objection or hearing request, identified by docket ID number EPA–HQ–OPP–2011–1028, by one of the following methods:

- *Federal eRulemaking Portal : http://www.regulations.gov* . Follow the online instructions for submitting comments. Do not submit electronically any information you consider to be (CBI) or other information whose disclosure is restricted by statute.
- *Mail:* OPP Docket, Environmental Protection Agency Docket Center (EPA/DC), (28221T), 1200 Pennsylvania Ave. NW., Washington, DC 20460–0001.
- *Hand Delivery:* To make special arrangements for hand delivery or delivery of boxed information, please follow the instructions at *http://www.epa.gov/dockets/contacts.htm.*

Additional instructions on commenting or visiting the docket, along with more information about dockets generally, is available at *http://www.epa.gov/dockets.*

II. Background and Statutory Findings

In the **Federal Register** of March 14, 2012 (77 FR 15012) (FRL–9335–9), EPA issued a notice pursuant to FFDCA section 408(d)(3), 21 U.S.C. 346a(d)(3), announcing the filing of a pesticide tolerance petition (PP 1F7940) by Conn & Smith, Inc., Agent, 6713 Catskill Road, Lorton, VA 22079, on behalf of Kaken Pharmaceutical Co., Ltd. The petition requested that 40 CFR 180.1285 be amended by expanding the current exemption to include all food commodities, thus establishing an exemption from the requirement of a tolerance for residues of polyoxin D zinc salt in or on all food commodities. This notice referenced a summary of the petition prepared by the petitioner Conn & Smith, Inc., on behalf of Kaken Pharmaceutical Co., Ltd., which is available in the docket, *http://www.regulations.gov.* There were no comments received in response to the notice of filing.

Section 408(c)(2)(A)(i) of FFDCA allows EPA to establish an exemption from the requirement for a tolerance (the legal limit for a pesticide chemical residue in or on a food) only if EPA determines that the exemption is ''safe.'' Section 408(c)(2)(A)(ii) of FFDCA defines ''safe'' to mean that ''there is a reasonable certainty that no harm will result from aggregate exposure to the pesticide chemical residue, including all anticipated dietary exposures and all other exposures for which there is reliable information.'' This includes exposure through drinking water and in residential settings, but does not include occupational exposure. Pursuant to FFDCA section 408(c)(2)(B), in establishing or maintaining in effect an exemption from the requirement of a tolerance, EPA must take into account the factors set forth in FFDCA section 408(b)(2)(C), which require EPA to give special consideration to exposure of infants and children to the pesticide chemical residue in establishing a tolerance and to ''ensure that there is a reasonable certainty that no harm will result to infants and children from aggregate exposure to the pesticide chemical residue. * * * '' Additionally, FFDCA section 408(b)(2)(D) requires that the Agency consider'' available information concerning the cumulative effects of such residues and other substances that have a common mechanism of toxicity.''

EPA performs a number of analyses to determine the risks from aggregate exposure to pesticide residues. First, EPA determines the toxicity of pesticides. Second, EPA examines exposure to the pesticide through food, drinking water, and through other exposures that occur as a result of pesticide use in residential settings.

III. Toxicological Profile

Consistent with FFDCA section 408(b)(2)(D), EPA has reviewed the available scientific data and other relevant information in support of this action and considered its validity, completeness and reliability, and the relationship of this information to human risk. EPA has also considered available information concerning the variability of the sensitivities of major identifiable subgroups of consumers, including infants and children.

EPA established a tolerance exemption for polyoxin D zinc salt in a final rule published in the **Federal Register** on November 19, 2008, (73 FR 69559) (FRL–8389–5), which supported the uses as a fungicide on almonds, cucurbit vegetables, fruiting vegetables, ginseng, grapes, pistachios, pome fruits, potatoes, and strawberries. The toxicological data submitted to support the previous tolerance exemption included the following: Acute (six-pack) toxicity, mutagenicity, subchronic (90-day oral), developmental, and chronic/oncogenicity studies. All of the studies/information submitted to support the previous tolerance exemption indicated a lack of toxicity hazards for mammals, and EPA concluded that there is a reasonable certainty of no harm to humans, including infants and children, from the proposed food uses of polyoxin D zinc salt. This amendment proposes to expand the tolerance exemption to include all food commodities when applied as a fungicide and used in accordance with good agricultural practices. In support of this expansion of the tolerance exemption, new data have been generated by the petitioner and reviewed by EPA to further address the developmental toxicity (OCSPP Guideline No. 870.3700) and mutagenicity (OCSPP Guideline Nos. 870.5100 and 870.5375) data requirements. The data are required when the use of the substance under widespread and commonly recognized practices may reasonably be expected to result in significant exposure to humans, specifically females of child-bearing age for the developmental toxicity data requirement. The rest of the toxicological profile as stated in the **Federal Register** of November 19, 2008, and referenced herein, has not changed. A copy of the November 19, 2008 final rule document (73 FR 69559) is located under docket ID number EPA–HQ–OPP–2008–0417. A copy of the risk assessment cited herein (See Ref.) is located under docket ID number EPA–HQ–OPP–2011–1028.

As discussed in the **Federal Register** of November 19, 2008 polyoxin D zinc salt is a brown musty smelling powder derived through the fermentation of the microbe *Streptomyces cacaoi var. asoensis* , which was isolated from a soil sample collected from Japan. This biochemical active ingredient has a non-toxic mode of action, which acts against fungi by inhibiting chitin growth in the cell walls, thus precluding the development of fungal colonies. Its effects are considered fungi-exclusive in that it has no mode of action relative to mammals and passes through mammalian digestive systems. Polyoxin D zinc salt does not persist in the

environment and has a well understood low toxicity profile.

As stated previously in this Unit (III), new toxicity data have been submitted in support of the request by the petitioner to expand the current tolerance exemption to cover all food commodities. These data include:

1. A prenatal developmental toxicity study; and

2. Two mutagenicity studies.

All new data, coupled with the data submitted to support the previous tolerance exemption (73 FR 69561), confirm a lack of human health hazard, as noted and reported in the original assessment of the tolerance exemption, associated with dietary exposures of polyoxin D zinc salt and fully demonstrate the lack of acute, subchronic, and chronic toxicity. Summaries of the new toxicological data submitted in support of the expansion of the tolerance exemption follow.

A. Mutagenicity

Two new mutagenicity studies were performed for polyoxin D zinc salt to support the expansion of the tolerance exemption. The mutagenicity studies as described herein, along with the mutagenicity studies submitted to support the previous tolerance exemption (73 FR 69561), confirm that polyoxin D zinc salt is not a mutagen and that consumption of food commodities that have been treated with this substance when used as a pesticide is safe and will not result in any harm to human health from dietary exposure.

1. A reverse gene mutation assay in bacteria Master Record Identification Number ((MRID) 48653313) using the technical grade of polyoxin D zinc salt, dissolved in dimethyl sulfoxide (DMSO), with and without metabolic S9 activation, showed no mutagenic effects or evidence of cytotoxicity or insolubility even at the limiting dose of 5,000 ug/plate (See Ref.). Therefore, polyoxin D zinc salt is considered to be non-mutagenic under the conditions of this assay.

2. An *in vitro* mammalian chromosome aberration test (MRID 48653314) using the technical grade of polyoxin D zinc salt, dissolved in DMSO, with and without metabolic S9 activation, showed clastogenic potential in Chinese hamster lung cells (CHL/IU) with and without activation (See Ref.). In Experiment I, polyoxin D zinc salt was tested up to dose levels that caused >50% cell lethality without activation (260 µg/mL) and with activation (1,600 µg/mL). Without activation, the frequencies of the metaphases with structural chromosome aberrations (excluding gaps) were 14.5% and 7.5% at test article concentrations of 186 and 260µg/mL, respectively. With activation, the frequency of metaphase cells with structural chromosome aberrations (excluding gaps) was 9.5% at a test article concentration of 1,600 µg/mL. The frequency of polyploid metaphase cells showed no increases either without or with activation. In Experiment II, a 24-hour continuous treatment without activation resulted in a 8.0% frequency of metaphases with structural chromosome aberrations (excluding gaps) at the concentration of 133 µg/mL. There were no increases in the frequency of polyploid metaphases.

Although the submitted *in vitro* mammalian chromosome aberration test showed clastogenic potential, the results were not reproducible at the dose levels reported in the experiment. In addition, the mutagenicity data submitted to support the previous tolerance exemption (73 FR 69562), which included three complimentary Tier I mutagenicity tests and a Tier II mammalian erythrocyte micronucleus *in vivo* test, showed no mutagenic effects, including no clastogenic potential (no chromosomal aberrations). Furthermore, the lack of systemic toxicity noted in the following developmental toxicity section (Unit III.B) and the fact that no effects were reported in the Tier III 2-generation reproduction study submitted for the previous tolerance exemption (73 FR 69562), indicate that polyoxin D zinc salt is not mutagenic or clastogenic. Therefore, based on the weight of evidence of the mutagenicity data submitted to support this expansion of the tolerance exemption and the previous tolerance exemption (73 FR 69561), the mutagenicity data and information are sufficient to confirm that polyoxin D zinc salt is not a mutagen, and that consumption of food commodities that have been treated with this substance when used as a pesticide is safe and will not result in any harm to human health from dietary exposure.

B. Developmental Toxicity

A new developmental study (MRID 48653315) was performed for polyoxin D zinc salt to support the expansion of the tolerance exemption. No treatment-related effects were observed in general appearance, body weight, adjusted for gravid uterine weight, weight gain, or food consumption in maternal rats at the doses tested (0, 100, 300, and 1,000 milligrams/kilograms bodyweight/day (mg/kg bw/day) (See Ref.). Necropsy observations showed that almost all rats (20/24) in the 1,000 mg/kg/day group highest dose tested (HDT) had thickening of the limiting ridge. Therefore, the lowest observed adverse effect level (LOAEL) for maternal toxicity of polyoxin D zinc salt in rats is 1,000 mg/kg bw/day based on gross lesions in the stomach (thickening of the limiting ridge). The no observed adverse effect level (NOAEL) for maternal toxicity is 300 mg/kg bw/day based on no effects observed at this dose. Although an effect of gross lesions in the stomach was found in maternal rats at the limit dose tested (1,000 mg/kg bw/day), there were no reported systemic effects in maternal rats at this dose. The effect in the stomach lining was limited to a localized gastric irritation due to the route of entry (oral gavage) at the limit dose tested (1,000 mg/kg bw/day), which is typical of the nature of the test substance.

For developmental toxicity, no treatment-related effects were observed on developmental parameters including gravid uterine weight, placental weight, mean numbers of corpora lutea and implantation sites, numbers of early and later resorptions (dead or resorbed embryos or fetuses), number of live fetuses per dam, implantation index, viability index, sex ratio, and male and female body weight. The incidence of external, visceral, and skeletal variations and anomalies were not affected by treatment of polyoxin D zinc salt. Based on no effects observed for developmental toxicity at any doses tested, the NOAEL for developmental toxicity is greater than 1,000 mg/kg bw/day HDT. The LOAEL was not identified for developmental toxicity, suggesting that the test animals could have tolerated a higher dose.

Based on the developmental toxicity data submitted for this expansion to the tolerance exemption, and the Tier III 2-generation reproduction study submitted for the previous tolerance exemption (73 FR 69562), which showed no reproductive effects at the limit dose tested, there are sufficient data and information to confirm that polyoxin D zinc salt is not a developmental toxicant, and that consumption of food commodities that have been treated with this substance when used as a pesticide is safe and will not result in any harm to human health from dietary exposure.

IV. Aggregate Exposures

In examining aggregate exposure, FFDCA section 408 directs EPA to consider available information concerning exposures from the pesticide residue in food and all other non-occupational exposures, including drinking water from ground water or

surface water and exposure through pesticide use in gardens, lawns, or buildings (residential and other indoor uses).

A. Dietary Exposure

Dietary risks to humans are considered negligible based on the lack of dietary toxicological endpoints for polyoxin D zinc salt and its non-toxic mode of action as a fungi-specific chitin synthetase inhibitor that passes through mammalian digestive systems. No significant acute, subchronic, mutagenic, immunotoxic, developmental, or chronic dietary toxicity hazards were identified in the studies submitted to support this expansion of the tolerance exemption or the previous tolerance exemption (73 FR 69562). Based on polyoxin D zinc salt's lack of dietary toxicity hazards for mammals, no aggregate dietary exposure concerns are expected.

1. *Food* . The petitioner submitted three nature of residue studies (MRIDs 486533–09 through –11) in plants (grapes, tomatoes, and lettuce) to support this expansion of the tolerance exemption. The three nature of residue studies represent EPA Crop Groups 13 (grapes), 08 (tomatoes), and 04 (lettuce). The total radioactive residue (TRR) levels measured were 0.520 parts per million (ppm) at day 1; 0.538 ppm at day 14; and 0.495 ppm at day 30 after the final application for the grape plant (See Ref.). For tomato plants, 0.073 ppm of polyoxin D was found 14 days after the last treatment on the tomato fruit. For lettuce, 0.025 ppm at day 7 and 0.107 ppm at day 14 were detected in the head of lettuce after final application.

In addition, a terrestrial exposure model (T-Rex) was performed for the previous tolerance exemption (73 FR 69562), which indicated that it is highly unlikely that there will be adverse effects resulting from the use of polyoxin D zinc salt via the oral route of exposure. EPA's T-Rex calculations delimit aggregate dietary consumption of residues to no more than 40 ppm, a level that is far below the HDT in any of the toxicity testing.

Based on the residue data submitted for this expansion of the tolerance exemption, and the T-Rex residue modeling data from the previous tolerance exemption (73 FR 69562), any residues found are far below any toxicological endpoints identified in this expansion of the tolerance exemption (developmental toxicity NOAEL greater than 1,000 mg/kg bw/day; maternal toxicity NOAEL of 300 mg/kg/day) or in the previous tolerance exemption (73 FR 69561). The previous tolerance exemption showed an acute oral toxicity median lethal dose (LD_{50}) greater than 10,000 mg/kg; a subchronic oral toxicity NOAEL of greater than 1,333 mg/kg/day and 119 mg/kg/day in female and male rats, respectively; a subchronic oral toxicity LOAEL of 1,166 mg/kg/day in male rats based on decreased body weight gain, food consumption, and food efficiency; and a chronic oral toxicity NOAEL 2,058.7 mg/kg bw/day in male rats and 2,469.8 mg/kg bw/day in female rats.

In summary, the residue and toxicity data demonstrate a lack of aggregate dietary risk that is sufficient to support this expansion of the tolerance exemption.

2. *Drinking water exposure* . As stated in the previous tolerance exemption (73 FR 69562), there is a small potential for trace amounts of polyoxin D zinc salt to enter drinking water sources after a significant rainfall, via surface water runoff, and/or via incidental spray drift. The petitioner submitted a photodegradation in water study (MRID 48653305) to support this tolerance exemption. The results of the study show that polyoxin D zinc salt has a net photolytic half-life of 0.4 days in sterile natural water (See Ref.) . Even if residues of polyoxin D zinc salt enter water sources, residues are expected to degrade and be so diluted as to be negligible. The data and information demonstrate a lack of aggregate dietary risk via drinking water and is sufficient to support this expansion of the tolerance exemption.

B. Other Non-Occupational Exposure

No new non-occupational exposure is expected to result from the new food uses of polyoxin D zinc salt. No health risks are expected from any non-occupational exposure to polyoxin D zinc salt based on the data submitted for the previous tolerance exemption (73 FR 69562) and for this expansion of the tolerance exemption.

1. *Dermal exposure* . No new non-occupational dermal exposures are expected to result from the new food uses of polyoxin D zinc salt resulting from this expansion of the tolerance exemption. Any new dermal exposure associated with this expansion of the tolerance exemption is expected to be occupational in nature.

2. *Inhalation exposure* . No new non-occupational inhalation exposures are expected to result from the new food uses of polyoxin D zinc salt resulting from this expansion of the tolerance exemption. Any new inhalation exposure associated with this expansion of the tolerance exemption is expected to be occupational in nature.

V. Cumulative Effects From Substances With a Common Mechanism of Toxicity

Section 408(b)(2)(D)(v) of FFDCA requires that, when considering whether to establish, modify, or revoke a tolerance, the Agency consider "available information concerning the cumulative effects of a particular pesticide's residues and other substances that have a common mechanism of toxicity."

EPA has not found polyoxin D zinc salt to share a common mechanism of toxicity with any other substances, and polyoxin D zinc salt does not appear to produce a toxic metabolite produced by other substances. For the purposes of this tolerance action, therefore, EPA has assumed that polyoxin D zinc salt does not have 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 EPA's Web site at *http://www.epa.gov/pesticides/cumulative.*

VI. Determination of Safety for U.S. Population, Infants and Children

FFDCA section 408(b)(2)(C) provides that EPA shall assess the available information about consumption patterns among infants and children, special susceptibility of infants and children to pesticide chemical residues, and the cumulative effects on infants and children of the residues and other substances with a common mechanism of toxicity. In addition, FFDCA section 408(b)(2)(C) provides that EPA shall apply an additional tenfold margin of safety for infants and children in the case of threshold effects to account for prenatal and postnatal toxicity and the completeness of the database unless EPA determines that a different margin of safety will be safe for infants and children. Margins of exposure safety, which are often referred to as uncertainty factors, are incorporated into EPA risk assessments either directly or through the use of a margin of exposure analysis, or by using uncertainty (safety) factors in calculating a dose level that poses no appreciable risk.

Relevant data and information submitted for the previous tolerance exemption (73 FR 69560) and for this expansion of the tolerance exemption indicate that polyoxin D zinc salt has negligible acute, subchronic, chronic, and developmental toxicity. Moreover, polyoxin D zinc salt is defined by its fungistatic non-toxic mode of action, and demonstrates no significant mammalian effect. Therefore, the

Agency concludes that there is a reasonable certainty that no harm will result to the U.S. population, including infants and children, from aggregate exposure to the residues of polyoxin D zinc salt. This includes all anticipated dietary exposures and all other exposures for which there is reliable information. EPA has arrived at this conclusion because the data and information available on polyoxin D zinc salt do not demonstrate toxic potential to mammals. Thus, there are no threshold effects of concern and, as a result, an additional margin of safety is not necessary.

VII. Other Considerations

A. Analytical Enforcement Methodology

An analytical method is not required for enforcement purposes for the reasons stated above, and because EPA is establishing an exemption from the requirement of a tolerance without any numerical limitation.

B. International Residue Limits

In making its tolerance decisions, EPA seeks to harmonize U.S. tolerances with international standards whenever possible, consistent with U.S. food safety standards and agricultural practices. EPA considers the international maximum residue limits (MRLs) established by the Codex Alimentarius Commission (Codex), as required by FFDCA section 408(b)(4). The Codex Alimentarius is a joint United Nations Food and Agriculture Organization/World Health Organization food standards program, and it is recognized as an international food safety standards-setting organization in trade agreements to which the United States is a party. EPA may establish a tolerance that is different from a Codex MRL; however, FFDCA section 408(b)(4) requires that EPA explain the reasons for departing from the Codex level.

The Codex has not established a MRL for polyoxin D zinc salt.

VIII. Conclusions

EPA concludes that there is a reasonable certainty that no harm will result to the U.S. population, including infants and children, from aggregate exposure to residues of polyoxin D zinc salt. Therefore, the existing exemption from the requirement of a tolerance for residues of polyoxin D zinc salt when used as a fungicide on almonds, cucurbit vegetables, fruiting vegetables, ginseng, grapes, pistachios, pome fruits, potatoes, and strawberries is amended by establishing an exemption from the requirement of a tolerance for residues of polyoxin D zinc salt in or on all food commodities when applied as a fungicide and used in accordance with good agricultural practices.

IX. References

The reference used in this document is in the OPP docket listed under docket ID EPA–HQ–OPP–2011–1028 and may be seen by accessing the *www.regulations.gov* Web site. A copy of the previous final rule published in the **Federal Register** on November 19, 2008, is in the OPP docket listed under docket ID EPA–HQ–OPP–2008–0417.

U.S. EPA. 2011. Memorandum from Manying Xue to Colin Walsh. Polyoxin D zinc salt (EPA Reg. #: 68173–1), Containing 23.8% of Polyoxin D Zinc Salt (Active Ingredient). Science Review of Product Chemistry, Residue Chemistry, Non-Target Organism and Toxicity Data in Support of label Amendment. U.S. Environmental Protection Agency Office of Pesticide Programs. May 11, 2012.

X. Statutory and Executive Order Reviews

This final rule establishes a tolerance under FFDCA section 408(d) in response to a petition submitted to the Agency. The Office of Management and Budget (OMB) has exempted these types of actions from review under Executive Order 12866, entitled ''Regulatory Planning and Review'' (58 FR 51735, October 4, 1993). Because this final rule has been exempted from review under Executive Order 12866, this final rule is not subject to Executive Order 13211, entitled ''Actions Concerning Regulations That Significantly Affect Energy Supply, Distribution, or Use'' (66 FR 28355, May 22, 2001) or Executive Order 13045, entitled ''Protection of Children from Environmental Health Risks and Safety Risks'' (62 FR 19885, April 23, 1997). This final rule does not contain any information collections subject to OMB approval under the Paperwork Reduction Act (PRA), 44 U.S.C. 3501 *et seq* ., nor does it require any special considerations under Executive Order 12898, entitled ''Federal Actions to Address Environmental Justice in Minority Populations and Low-Income Populations'' (59 FR 7629, February 16, 1994).

Since tolerances and exemptions that are established on the basis of a petition under FFDCA section 408(d), such as the tolerance exemption in this final rule, do not require the issuance of a proposed rule, the requirements of the Regulatory Flexibility Act (RFA) (5 U.S.C. 601 *et seq* .), do not apply.

This final rule directly regulates growers, food processors, food handlers, and food retailers, not States or tribes, nor does this action alter the relationships or distribution of power and responsibilities established by Congress in the preemption provisions of FFDCA section 408(n)(4). As such, the Agency has determined that this action will not have a substantial direct effect on States or tribal governments, on the relationship between the national government and the States or tribal governments, or on the distribution of power and responsibilities among the various levels of government or between the Federal Government and Indian tribes. Thus, the Agency has determined that Executive Order 13132, entitled ''Federalism'' (64 FR 43255, August 10, 1999) and Executive Order 13175, entitled ''Consultation and Coordination with Indian Tribal Governments'' (65 FR 67249, November 9, 2000) do not apply to this final rule. In addition, this final rule does not impose any enforceable duty or contain any unfunded mandate as described under Title II of the Unfunded Mandates Reform Act of 1995 (UMRA) (2 U.S.C. 1501 *et seq* .).

This action does not involve any technical standards that would require Agency consideration of voluntary consensus standards pursuant to section 12(d) of the National Technology Transfer and Advancement Act of 1995 (NTTAA) (15 U.S.C. 272 note).

XI. Congressional Review Act

Pursuant to the Congressional Review Act (5 U.S.C. 801 *et seq* .), EPA will submit a report containing this rule and other required information to the U.S. Senate, the U.S. House of Representatives, and the Comptroller General of the United States prior to publication of the rule in the **Federal Register**. This action is not a ''major rule'' as defined by 5 U.S.C. 804(2).

List of Subjects in 40 CFR Part 180

Environmental protection, Administrative practice and procedure, Agricultural commodities, Pesticides and pests, Reporting and recordkeeping requirements.

Dated: August 29, 2012.

Keith A. Matthews,

Director, Biopesticides and Pollution Prevention Division, Office of Pesticide Programs.

Therefore, 40 CFR chapter I is amended as follows:

PART 180—[AMENDED]

■ 1. The authority citation for part 180 continues to read as follows:

Authority: 21 U.S.C. 321(q), 346a and 371.

■ 2. Section 180.1285 is revised to read as follows:

§ 180.1285 Polyoxin D zinc salt; exemption from the requirement of a tolerance.

An exemption from the requirement of a tolerance is established for the residues of polyoxin D zinc salt in or on all food commodities when applied as a fungicide and used in accordance with good agricultural practices.

[FR Doc. 2012–22315 Filed 9–11–12; 8:45 am]

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ENVIRONMENTAL PROTECTION AGENCY

40 CFR Part 180

[EPA–HQ–OPP–2011–0433; FRL–9359–6]

Dinotefuran; Pesticide Tolerances

AGENCY: Environmental Protection Agency (EPA).

ACTION: Final rule.

SUMMARY: This regulation establishes tolerances for residues of dinotefuran in or on multiple commodities which are identified and discussed later in this document. Also, due to the tolerances established by this document, the Agency is removing the existing tolerances for grape and potato as unnecessary. Interregional Research Project Number 4 (IR–4) requested these tolerances under the Federal Food, Drug, and Cosmetic Act (FFDCA).

DATES: This regulation is effective September 12, 2012. Objections and requests for hearings must be received on or before November 13, 2012, and must be filed in accordance with the instructions provided in 40 CFR part 178 (see also Unit I.C. of the **SUPPLEMENTARY INFORMATION**).

ADDRESSES: The docket for this action, identified by docket identification (ID) number EPA–HQ–OPP–2011–0433, is available at *http://www.regulations.gov* or at the Office of Pesticide Programs Regulatory Public Docket (OPP Docket) in the Environmental Protection Agency Docket Center (EPA/DC), EPA West Bldg., Rm. 3334, 1301 Constitution Ave. NW., Washington, DC 20460–0001. The Public Reading Room is open from 8:30 a.m. to 4:30 p.m., Monday through Friday, excluding legal holidays. The telephone number for the Public Reading Room is (202) 566–1744, and the telephone number for the OPP Docket is (703) 305–5805. Please review the visitor instructions and additional information about the docket available at *http://www.epa.gov/dockets.*

FOR FURTHER INFORMATION CONTACT: Andrew Ertman, Registration Division, Office of Pesticide Programs, Environmental Protection Agency, 1200 Pennsylvania Ave., NW., Washington, DC 20460–0001; telephone number: (703) 308–9367; email address: *ertman.andrew@epa.gov.*

SUPPLEMENTARY INFORMATION:

I. General Information

A. Does this action apply to me?

You may be potentially affected by this action if you are an agricultural producer, food manufacturer, or pesticide manufacturer. The following list of North American Industrial Classification System (NAICS) codes is not intended to be exhaustive, but rather provides a guide to help readers determine whether this document applies to them. Potentially affected entities may include:

- Crop production (NAICS code 111).
- Animal production (NAICS code 112).
- Food manufacturing (NAICS code 311).
- Pesticide manufacturing (NAICS code 32532).

B. How can I get electronic access to other related information?

You may access a frequently updated electronic version of EPA's tolerance regulations at 40 CFR part 180 through the Government Printing Office's e-CFR site at http://ecfr.gpoaccess.gov/cgi/t/text/text-idx?&c=ecfr&tpl=/ecfrbrowse/Title40/40tab_02.tpl.

C. How can I file an objection or hearing request?

Under FFDCA section 408(g), 21 U.S.C. 346a, any person may file an objection to any aspect of this regulation and may also request a hearing on those objections. You must file your objection or request a hearing on this regulation in accordance with the instructions provided in 40 CFR part 178. To ensure proper receipt by EPA, you must identify docket ID number EPA–HQ–OPP–2011–0433 in the subject line on the first page of your submission. All objections and requests for a hearing must be in writing, and must be received by the Hearing Clerk on or before November 13, 2012. Addresses for mail and hand delivery of objections and hearing requests are provided in 40 CFR 178.25(b).

In addition to filing an objection or hearing request with the Hearing Clerk as described in 40 CFR part 178, please submit a copy of the filing (excluding any Confidential Business Information (CBI)) for inclusion in the public docket. Information not marked confidential pursuant to 40 CFR part 2 may be disclosed publicly by EPA without prior notice. Submit the non-CBI copy of your objection or hearing request, identified by docket ID number EPA–HQ–OPP–2011–0433, by one of the following methods:

- *Federal eRulemaking Portal: http://www.regulations.gov.* Follow the online instructions for submitting comments. Do not submit electronically any information you consider to be CBI or other information whose disclosure is restricted by statute.
- *Mail:* OPP Docket, Environmental Protection Agency Docket Center (EPA/DC), (28221T), 1200 Pennsylvania Ave. NW., Washington, DC 20460–0001.
- *Hand Delivery:* To make special arrangements for hand delivery or delivery of boxed information, please follow the instructions at *http://www.epa.gov/dockets/contacts.htm.*

Additional instructions on commenting or visiting the docket, along with more information about dockets generally, is available at *http://www.epa.gov/dockets.*

II. Summary of Petitioned-For Tolerance

In the **Federal Register** of September 7, 2011 (76 FR 55329) (FRL–8886–7), EPA issued a notice pursuant to FFDCA section 408(d)(3), 21 U.S.C. 346a(d)(3), announcing the filing of a pesticide petition (PP 1E7863) by IR–4, 500 College Rd. East, Suite 201 W, Princeton, NJ 08540. The petition requested that 40 CFR 180.603 be amended by establishing tolerances for residues of the insecticide dinotefuran, (*RS*)-1-methyl-2-nitro-3-((tetrahydro-3-furyl)methyl)guanidine, including its metabolites and degradates, in or on berry, low growing, except strawberry, subgroup 13–07H at 0.2 parts per million (ppm); watercress at 5.0 ppm; onion, green, subgroup 3–07B at 6.0 ppm; onion, bulb, subgroup 3–07A at 0.07 ppm; peach at 0.9 ppm; vegetable, tuberous and corm, subgroup 1C at 0.05 ppm; fruit, small, vine climbing, except fuzzy kiwifruit, subgroup 13–07F at 0.9 ppm; and tea, plucked leaves at 25.0 ppm. That notice referenced a summary of the petition prepared by Mitsui Chemicals Agro, Inc., the registrant, which is available in the docket, *http://www.regulations.gov.* There were no comments received in response to the notice of filing.

Also, due to the tolerances established by this document, the following existing tolerances are being removed as unnecessary: Grape and potato.

Based upon review of the data supporting the petition, EPA has

E-mail from EPA that defines the scope of "all food commodities"

Subject: Re: Polyoxin D Zinc Salt: EPA review confusion
X-KeepSent: D347C55A:FE32DA54-85257A76:00605592;
type=4; name=$KeepSent
To: Cindy Smith <cindy@connsmith.com>
X-Mailer: Lotus Notes Release 8.5 December 05, 2008
From: Colin Walsh <Walsh.Colin@epamail.epa.gov>
Date: Tue, 11 Sep 2012 13:36:33 -0400
X-MIMETrack: Serialize by Router on EPAHUB13/USEPA/US(Release 8.5.2FP2|March 22, 2011) at
09/11/2012 01:36:30 PM
X-pstn-levels: (S:99.90000/99.90000 CV:99.9000 FC:95.5390 LC:95.5390 R:95.9108 P:95.9108 M:97.0282 C:98.6951)
X-pstn-dkim: 0 skipped:not-enabled
X-pstn-settings: 3 (1.0000:1.0000) s cv gt3 gt2 gt1 r p m c
X-pstn-addresses: from <Walsh.Colin@epamail.epa.gov> [107/4]
X-MS-Exchange-Organization-AuthSource: Portal-EX10.Portal.Local
X-MS-Exchange-Organization-AuthAs: Anonymous
X-Brightmail-Tracker: AAAAAA==
X-MS-Exchange-Organization-AVStamp-Mailbox: SYMANTEC;455737472;0;info

Hi Cindy,

I was just able to confirm that "in or on all food commodities" includes pre-harvest and post-harvest uses and all food and feed uses unless we specifically indicate in the rule that one of those uses is not allowed. Since we do not have any exceptions in the rule, all of those uses are allowed for polyoxin D zinc salt. Please let me know if you have any more questions on this action.

Regards,

Colin

Colin G. Walsh, M.S.
Biologist, Biochemical Pesticides Branch
Biopesticides and Pollution Prevention Division (7511P)
Office of Pesticide Programs
U.S. Environmental Protection Agency
walsh.colin@epa.gov
(703) 308-0298 (phone)
(703) 305-0118 (fax)
http://www.epa.gov/pesticides/

Cindy Smith ---09/11/2012 01:29:02 PM---Thanks. At 12:01 PM 9/11/2012, you wrote:

From: Cindy Smith <cindy@connsmith.com>
To: Colin Walsh/DC/USEPA/US@EPA
Date: 09/11/2012 01:29 PM
Subject: Re: Polyoxin D Zinc Salt: EPA review confusion

Thanks.

At 12:01 PM 9/11/2012, you wrote:

EPA stamped "ACCEPTED" label for Polyoxin D Zinc Salt Technical that expands uses to include production of formulations made for use on all food and feed crops and for pre-harvest and post-harvest use

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

OFFICE OF CHEMICAL SAFETY
AND POLLUTION PREVENTION

Kaken Pharmaceutical Co., Ltd.
c/o Cynthia Ann Smith
Conn & Smith, Inc.
6713 Catskill Road
Lorton, VA 22079-1113

AUG 2 9 2012

Subject: Registration Amendment to expand the tolerance exemption to all food commodities for the active ingredient, polyoxin D zinc salt, and add all food commodities to the label.
Polyoxin D Zinc Salt Technical
EPA Reg. No.: 68173-1
Your submission dated November 15, 2011
Decision Number: 457591, PRIA Category B631

Dear Ms. Smith:

The amendment referred to above submitted in connection with registration under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) section 3(c)(5), is acceptable provided that you:

1) Submit and/or cite all data required for registration/reregistration of your product under FIFRA section 3(c)(5) when the Agency requires all registrants of similar products to submit such data.

2) Submit two (2) copies of your final printed labeling before you release the product for shipment. Final printed labeling means the label or labeling of the product when distributed or sold. Clearly legible reproductions or photo reductions will be accepted for unusual labels, such as those silk-screened directly onto glass or metal containers or large bags or drum labels.

If these conditions are not complied with, the registration will be subject to cancellation in accordance with FIFRA section 6(e). Your release for shipment of the product bearing the amended labeling constitutes acceptance of these conditions. A stamped copy of the label is enclosed for your records. Should you have any questions, you may contact Mr. Colin Walsh directly at (703) 308-0298 or via email at walsh.colin@epa.gov.

Sincerely,

Linda A. Hollis, Chief
Biochemical Pesticides Branch
Biopesticides and Pollution
Prevention Division (7511P)

Polyoxin D Zinc Salt Technical (EPA Reg. No. 68173-1)
August 24, 2012 revised proposed label based upon comments received by email on August 23, 2012 regarding the November 15, 2011 proposed amended label to permit use on all for and feed crops
Changes implemented.
Page 1 of 3
068173-00001.20120824.all crops.pdf

ACCEPTED

AUG 29 2012

Under the Federal Insecticide, Fungicide, and Rodenticide Act, as amended, for the pesticide registered under EPA Reg. No. 68173-1

Polyoxin D Zinc Salt Technical

For Manufacturing Use Only

GROUP 19 FUNGICIDE

Active Ingredient:	
Polyoxin D zinc salt (1:1)[1], Zinc 5-[[2-amino-5-*O*-(aminocarbonyl)-2-deoxy-L-xylonyl]amino]-1-(5-carboxy-3,4-dihydro-2,4-dioxo-1(2*H*)-pyrimidinyl)-1,5-dideoxy-ß-D-allofuranuronate	23.8%
Other Ingredients:	76.2%
Total:	100.0%

[1] Equivalent to 21.1% polyoxorim and 2.65% metallic zinc.

KEEP OUT OF REACH OF CHILDREN
CAUTION

FIRST AID	
If on skin or clothing	• Take off contaminated clothing. • Rinse skin immediately with plenty of water for 15-20 minutes. • Call a poison control center of doctor for treatment advice.
If in eyes	• Hold eye open and rinse slowly and gently with water for 15-20 minutes. • Remove contact lenses, if present, after the first 5 minutes, then continue rinsing eye. • Call a poison control center or doctor for treatment advice.
If swallowed	• Call a poison control center or doctor immediately for treatment advice. • Have person sip a glass of water if able to swallow. • Do not induce vomiting unless told to by a poison control center or doctor. • Do not give anything by mouth to an unconscious person.
If inhaled	• Move person to fresh air. • If person is not breathing, call 911 or an ambulance, then give artificial respiration, preferable by mouth-to-mouth, if possible. • Call a poison control center or doctor for further treatment advice.

HOTLINE NUMBER

Have the product container or label with you when calling a poison control center or doctor, or going for treatment.

FOR 24-HOUR EMERGENCY MEDICAL ASSISTANCE:

Call CHEMTREC at 1-800-424-9300 or POISON CONTROL CENTER at 1-800-222-1222 or 1-703-527-3887 if calling from outside of the U.S.

Polyoxin D Zinc Salt Technical (EPA Reg. No. 68173-1)
August 24, 2012 revised proposed label based upon comments received by email on August 23, 2012 regarding the November 15, 2011 proposed amended label to permit use on all for and feed crops
Changes implemented.
Page 2 of 3
068173-00001.20120824.all crops.pdf

PRECAUTIONARY STATEMENTS
HAZARDS TO HUMANS AND DOMESTIC ANIMALS

CAUTION: Causes moderate eye irritation. Harmful if absorbed through the skin, swallowed or inhaled. Avoid contact with skin, eyes or clothing. Avoid breathing dust. Wash thoroughly with soap and water after handling and before eating, drinking, chewing gum, using tobacco, or using the toilet.

ENVIRONMENTAL HAZARDS

This pesticide is moderately toxic to aquatic invertebrates and fish. Do not discharge effluent containing this product into lakes, streams, ponds, estuaries, oceans, or other waters unless in accordance with the requirements of a National Pollutant Discharge Elimination System (NPDES) permit and the permitting authority has been notified in writing prior to discharge. Do not discharge effluent containing this product to sewer systems without previously notifying the local sewage treatment plant authority. For guidance contact your State Water Board or Regional Office of the EPA.

DIRECTIONS FOR USE

It is a violation of Federal law to use this product in a manner inconsistent with its labeling.

Polyoxin D Zinc Salt Technical is for manufacturing use only for the production of fungicide formulations for use on all food and feed crops (pre-harvest and post-harvest), ornamentals, golf courses, residential lawns, parks, and commercial and institutional grounds.

STORAGE AND DISPOSAL

Do not contaminate water, food or feed by storage or disposal.
PESTICIDE STORAGE: Store in dry place away from food or feed.
PESTICIDE DISPOSAL: Wastes resulting from the use of this product may be disposed of on site or at an approved waste disposal facility.
CONTAINER HANDLING: Nonrefillable container. Do not reuse or refill this container. Completely empty bag into manufacturing equipment. Then dispose of empty bag in a sanitary landfill or by incineration, or, if allowed by State and local authorities, by burning. If burned, stay out of smoke.

FOR 24-HOUR CHEMICAL EMERGENCY ASSISTANCE:
(Spill, leak, fire, exposure or accident), call CHEMTREC 1-800-424-9300
or 1-703-527-3887 if calling from outside of the U.S.

Polyoxin D Zinc Salt Technical (EPA Reg. No. 68173-1)
August 24, 2012 revised proposed label based upon comments received by email on August 23, 2012 regarding the November 15, 2011 proposed amended label to permit use on all for and feed crops
Changes implemented.
Page 3 of 3
068173-00001.20120824.all crops.pdf

WARRANTY AND DISCLAIMER STATEMENT

1. Kaken Pharmaceutical Co., Ltd. ("Kaken") warrants that this product conforms to the chemical description on the label and is reasonably fit for the purposes stated in the Directions for Use, subject to the inherent risks described above, when used in accordance with the Directions for Use under normal conditions.

2. This warranty does not extend to the use of this product contrary to label instructions or under conditions not reasonably foreseeable to Kaken, and is subject to the inherent risks described above. **TO THE EXTENT CONSISTENT WITH APPLICABLE LAW, KAKEN DISCLAIMS ALL OTHER WARRANTIES, EXPRESSED OR IMPLIED, INCLUDING ANY WARRANTY OF MERCHANTABILITY OR FITNESS FOR A PARTICULAR PURPOSE. TO THE EXTENT CONSISTENT WITH APPLICABLE LAW, KAKEN, MANUFACTURER, AND SELLER DISCLAIM AND SHALL NOT BE LIABLE FOR ANY SPECIAL, INCIDENTAL, INDIRECT, OR CONSEQUENTIAL DAMAGES RESULTING FROM THE USE, HANDLING, APPLICATION, STORAGE OR DISPOSAL OF THIS PRODUCT OR FOR DAMAGES IN THE NATURE OF PENALTIES, AND THE USER AND BUYER WAIVE ANY RIGHT THAT THEY MAY HAVE TO SUCH DAMAGES. NO AGENT, REPRESENTATIVE OR EMPLOYEE OF KAKEN IS AUTHORIZED TO MAKE ANY WARRANTY, GUARANTEE OR REPRESENTATION BEYOND THOSE CONTAINED HEREIN OR TO MODIFY THE WARRANTIES CONTAINED HEREIN.**

3. **TO THE EXTENT CONSISTENT WITH APPLICABLE LAW, THE EXCLUSIVE REMEDY OF THE USER OR BUYER, AND THE TOTAL LIABILITY OF KAKEN, MANUFACTURER, AND SELLER, SHALL BE LIMITED TO THE PURCHASE PRICE PAID, OR AT KAKEN'S ELECTION, THE REPLACEMENT OF THE PRODUCT.**

EPA Reg. No: 68173-1
EPA Est. No: 68173-JP-001

Net Contents:

Produced by:
Kaken Pharmaceutical Co., Ltd.
Agrochemicals & Animal Health Products Division
28-8 Honkomagome 2-chome
Bunkyo, Tokyo 113-8650, Japan

EPA stamped "ACCEPTED" label for VEGGIETURBO 5SC Suspension Concentrate Fungicide

U.S. ENVIRONMENTAL PROTECTION AGENCY
Office of Pesticide Programs
Biopesticides and Pollution Prevention Division (7511P)
1200 Pennsylvania Avenue NW
Washington, DC 20460

NOTICE OF PESTICIDE:
_X_ Registration
___ Reregistration
(under FIFRA, as amended)

EPA Reg. Number: 68173-4

Date of Issuance: SEP 27 2012

Term of Issuance: **Unconditional**

Name of Pesticide Product:
Veggieturbo 5SC
Suspension Concentrate
Fungicide

Name and Address of Registrant (include ZIP Code):

Kaken Pharmaceutical Co., Ltd.
Agrochemicals & Animal Health Products 28-8
Honkomagome 2-chome
Bunkyo-ku
Tokyo 113-8650
Japan

Note: Changes in labeling differing in substance from that accepted in connection with this registration must be submitted to and accepted by the Biopesticides and Pollution Prevention Division prior to use of the label in commerce. In any correspondence on this product always refer to the above EPA registration number.

On the basis of information furnished by the registrant, the above named pesticide is hereby registered under the Federal Insecticide, Fungicide and Rodenticide Act.

Registration is in no way to be construed as an endorsement or recommendation of this product by the Agency. In order to protect health and the environment, the Administrator, on his/her motion, may at any time suspend or cancel the registration of a pesticide in accordance with the Act. The acceptance of any name in connection with the registration of a product under this Act is not to be construed as giving the registrant a right to exclusive use of the name or to its use if it has been covered by others.

This registration does not eliminate the need for continual reassessment of the pesticide. If EPA determines at any time, that additional data are required to maintain in effect an existing registration, the Agency will require submission of such data under section 3(c)(2)(B) of FIFRA. This product is unconditionally registered in accordance with FIFRA Sec. 3(c)(5) provided you:

1. Submit and/or cite all data required for registration of your product under FIFRA section 3(c)(5) when the Agency requires all registrants of similar products to submit such data.
2. Revise the EPA Registration Number to read, "EPA Reg. No. 68173-4".
3. Submit within 1 year after the Date of Registration acceptable data packages for Guideline Studies: Storage Stability study (OPPTS GLN: 830.6317) and Corrosion Characteristics study (OPPTS GLN: 830.6320) for this product.
4. Submit two (2) copies of the final printed labeling before you release the product for shipment.

A stamped copy of the label is enclosed for your records.

Signature of Approving Official:

Daniel A. Helfgott, Acting Associate Director,
Biopesticides and Pollution Prevention Division

Date: 9/27/12

EPA Form 8570-6

068173-0000U.20120927.Changes_IMPLEMENTED.pdf
VEGGIETURBO 5SC (EPA File Symbol 68173-U) • Page 1 of 19
September 27, 2012 Revised Proposed Master Label
Updates the September 20, 2012 proposed label directions for use tables.
Changes IMPLEMENTED

[Front Panel]

GROUP 19 FUNGICIDE

VEGGIETURBO™ 5SC

Suspension Concentrate Fungicide

Optional text:
For Control of Fungal Diseases of Listed Vegetable and Fruits Crops

For Control of Fungal Diseases of Grapes, Strawberries, and Other Small Fruits

Active Ingredient	
Polyoxin D zinc salt	5.0%
Other Ingredients	95.0%
Total	100.0%

Contains 7.03 ounces of active ingredient per gallon.

KEEP OUT OF REACH OF CHILDREN

CAUTION

See back panel for additional precautionary statements.
[Alternate statement for 1000 Liter container:]
See below for additional precautionary statements.

Produced by:
Kaken Pharmaceutical Co., Ltd.
28-8, Honkomagome 2-chome, Bunkyo-ku,
Tokyo, JAPAN 113-8650

EPA Reg. No. 68173-__
EPA Est. No. _____

NET CONTENTS: 1 Quart (32 Fluid Ounces)
1 Gallon (128 Fluid Ounces)
2.5 Gallons (320 Fluid Ounces)
266 Gallons (1000 Liters)

ACCEPTED

SEP 27 2012

Under the Federal Insecticide, Fungicide, and Rodenticide Act, as amended, for the pesticide registered under EPA Reg. No. 68173-4

068173-0000U.20120927.Changes_IMPLEMENTED.pdf
VEGGIETURBO 5SC (EPA File Symbol 68173-U) • Page 2 of 19
September 27, 2012 Revised Proposed Master Label
Updates the September 20, 2012 proposed label directions for use tables.
Changes IMPLEMENTED

[Back Panel]

PRECAUTIONARY STATEMENTS
HAZARDS TO HUMANS & DOMESTIC ANIMALS

Caution. Prolonged or frequently repeated skin contact may cause allergic reactions in some individuals. Avoid contact with skin and clothing. Wash thoroughly with soap and water after handling and before eating, drinking, chewing gum, using tobacco, or using the toilet. Remove and wash contaminated clothing before reuse.

Optional Statements (EPA Category IV toxicity for acute oral, acute dermal, acute inhalation, eye irritation and dermal irritation)	
FIRST AID	
IF ON SKIN OR CLOTHING:	• *Take off contaminated clothing.* • *Rinse skin immediately with plenty of water for 15-20 minutes.* • *Call a poison control center or doctor for treatment advice.*
IF IN EYES:	• *Hold eye open and rinse slowly and gently with water for 15-20 minutes.* • *Remove contact lenses, if present, after the first 5 minutes, then continue rinsing eye.* • *Call a poison control center or doctor for further treatment advice.*
IF SWALLOWED:	• *Call a poison control center or doctor immediately for treatment advice.* • *Have person sip a glass of water if able to swallow.* • *Do not induce vomiting unless told to do so by the poison control center or doctor.* • *Do not give anything to an unconscious person.*
IF INHALED:	• *Move person to fresh air.* • *If person is not breathing, call 911 or an ambulance, then give artificial respiration, preferably mouth-to-mouth if possible.* • *Call a poison control center or doctor for further treatment advice.*
HOTLINE NUMBERS *Have the product container or label with you when calling a poison control center or doctor, or going for treatment. FOR 24-HOUR EMERGENCY MEDICAL ASSISTANCE, call 1-800-255-3924.*	

PERSONAL PROTECTIVE EQUIPMENT (PPE)

All mixers, loaders, applicators and other handlers must wear:

- Long-sleeved shirt and long pants;
- Socks;
- Shoes; and
- Chemical-resistant gloves.

Follow manufacturer's instructions for cleaning and maintaining PPE. If no instructions are available, use detergent and hot water for washables. Keep and wash PPE separately from other laundry. When handlers use closed systems, enclosed cabs, or aircraft in a manner that meets requirements listed in the Worker Protection Standard (WPS) for agricultural pesticides, the handler PPE requirements may be reduced or modified as specified in the WPS.

USER SAFETY RECOMMENDATIONS

Users should:

- Remove clothing/PPE immediately if pesticides get inside. Then wash thoroughly and put on clean clothing.
- Remove PPE immediately after handling this product. Wash the outside of gloves before removing. As soon as possible, wash thoroughly and change into clean clothing.

ENVIRONMENTAL HAZARDS

[For 1 liter, 1 gallon and 2.5 gallon containers:]
For terrestrial use. This pesticide is moderately toxic to aquatic invertebrates and fish. Do not apply directly 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. Do not allow runoff into lakes, streams, ponds or public waterways. Drift and runoff may be hazardous to aquatic organisms in water adjacent to treated areas. Observe the most restrictive labeling limitations and precautions of all products used in mixtures.

[For 1000 liter container:]
For terrestrial use. This pesticide is moderately toxic to aquatic invertebrates and fish. Do not apply directly 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. Do not allow runoff into lakes, streams, ponds or public waterways. Drift and runoff may be hazardous to aquatic organisms in water adjacent to treated areas. Observe the most restrictive labeling limitations and precautions of all products used in mixtures. Do not discharge effluent containing this product into lakes, streams, ponds, estuaries, oceans, or other waters unless in accordance with the requirements of a National Pollutant Discharge Elimination System (NPDES) permit and the permitting authority has been notified in writing prior to discharge. Do not discharge effluent containing this product to sewer systems without previously notifying the local sewage treatment plant authority. For guidance contact your State Water Board or Regional Office of the EPA.

GENERAL INFORMATION

VEGGIETURBO 5SC can be applied as a preventative or curative treatment in conjunction with good management practices.
VEGGIETURBO 5SC can be used alone or, when diseases not specified on this label are present or expected, in combination and/or rotation with other appropriately labeled fungicides as a tool for integrated disease management in labeled agricultural crops. See "Mixing and Handling Instructions" below for additional information.
Preharvest Interval (PHI) = 0 days. VEGGIETURBO 5SC is exempt from the requirement for residue tolerance and therefore can be applied up to and including the day of harvest.

RESISTANCE MANAGEMENT RECOMMENDATIONS

VEGGIETURBO 5SC contains a fungicide classified in FRAC target site of action Group 19. Fungal isolates with acquired resistance to Group 19 may eventually dominate the fungal population if Group 19 fungicides are used repeatedly in the same field or in successive years as the primary method of control for targeted species. This may result in partial or total loss of control of those species by VEGGIETURBO 5SC or other Group 19 Fungicides.

The following actions may prevent or delay fungicide resistance:

- Avoid consecutive use of VEGGIETURBO 5SC or other Group 19 fungicides against the same pathogens.
- Use tank-mixes or premixes with fungicides from different target site of action Groups. Do this only with products that are registered for the same use and are effective at the tank mix or premix rate against the target pathogen(s).
- Use fungicides as part of a comprehensive Integrated Pest Management (IPM) program.
- Monitor treated fungal populations for loss of field efficacy.

Contact your local extension specialist, certified crop advisor, and/or manufacture representative for fungicide resistance management and/or IPM recommendations for specific crops and resistant pathogens.

DIRECTIONS FOR USE

It is a violation of Federal law to use this product in a manner inconsistent with its labeling.

For any requirements specific to your State or Tribe, consult the State or Tribal agency responsible for pesticide regulation.

Do not apply this product in a way that will contact workers or other persons, either directly or through drift. Only protected handlers may be in the area during application.

AGRICULTURAL USE REQUIREMENTS

Use this product only in accordance with its labeling and with the Worker Protection Standard 40 CFR Part 170. This standard contains requirements for the protection of agricultural workers on farms, forests, nurseries, and greenhouses and handlers of agricultural pesticides. It contains requirements for training, decontamination, notification, and emergency assistance. It also contains specific instructions and exceptions pertaining to the statements on this label about personal protective equipment (PPE), and restricted entry intervals. The requirements in this box only apply to uses of this product that are covered by the Worker Protection Standard.

Do not enter or allow worker entry into treated areas during the restricted entry interval (REI) of 4 hours unless wearing appropriate PPE.

PPE required for early entry to treated areas that is permitted under the Worker Protection Standard and that involves contact with anything that has been treated, such as plants, soil or water is: coveralls, socks, shoes, and chemical-resistant gloves.

Low rate (3.75 fl. oz./acre) may be used for preventative applications before onset of visible disease, in periods of low disease pressure, or in a tank mix with other fungicides for resistance management. Use higher rates (6.5 to 13.0 fl. oz./acre) when disease pressure is high, or in stand-alone applications.

MIXING AND APPLICATION INSTRUCTIONS

VEGGIETURBO 5SC may be applied by ground or aerial spray equipment, as a soil drench, or by chemigation through sprinklers or drip irrigation. See the table below for information on application methods and timing for specific crops and diseases.

For spray application, mix VEGGIETURBO 5SC in water and apply as a spray to foliage, fruit, or other above-ground plant parts. For optimum control of labeled diseases, apply in sufficient volume of water to provide thorough coverage with minimal run-off.

See "Chemigation Instructions" below for information about applying VEGGIETURBO 5SC through irrigation systems.

[For 1 quart, 1 gallon and 2.5 gallon containers:]
Mixing instructions for VEGGIETURBO 5SC:

- *Shake well before use.*
- *Fill tank with water to ½ of the intended final volume.*
- *Start agitation of the spray tank.*
- *Add the appropriate amount of product to the tank according to the rates in this label.*
- *Agitate to ensure thorough mixing while adding the remaining required water.*
- *Do not allow the mixture to stand without agitation.*
- *Mix only the amount of solution needed to treat the desired area.*

[For 1000 Liter container:]
Thoroughly agitate product when product is in use.

When tank mixing VEGGIETURBO 5SC with other products, observe all precautions and limitations on each separate product label.

When planning to mix this product with others, it advisable to conduct a "jar test" to determine the physical compatibility of this product with the others. Using a quart jar, add the products (with agitation) to approximately one quart of water in the proportions they will appear in the final mixture. Add dry formulations first, followed by flowables, then emulsifiable concentrates like VEGGIETURBO 5SC last. After thorough mixing, allow this mixture to stand for 5 minutes. If the combination remains mixed or can be readily remixed, it is physically compatible. Once compatibility has been proven, use the same sequence for adding required ingredients to the tank.

To assess the potential for phytotoxicity, test tank mixtures on a small number of plants prior to more widespread application.

If more applications or shorter intervals than indicated in the table below are needed to maintain disease control, alternate VEGGIETURBO 5SC with other fungicides having different modes of action to avoid or slow development of pathogen resistance. See "Resistance Management Recommendations" above for more information.

Use of an adjuvant may enhance spray coverage of dense crop canopy, or plants that are difficult to

wet due to waxy or hairy surfaces. Use only adjuvants that are labeled for such uses. Refer to "Mixing and Application Instructions" above for information on testing physical compatibility of VEGGIETURBO 5SC with other products.

BANDED (IN-FURROW) APPLICATION

Use the table below to determine the correct application rate in fluid ounces of product per 1,000 row feet based on row spacing and desired rate per acre. Mix the required amount of VEGGIETURBO 5SC in water and apply as banded spray (4" to 6" wide) or seedline drench centered over the planting furrow. Apply to soil immediately before seeding or directly over seeds in the furrow just before they are covered with soil. The volume of water required per acre or per 1,000 row feet will depend on the application equipment used. Consult your local cooperative extension service if you need assistance calibrating band spraying equipment.

Rates for banded (in-furrow) application: Find desired application rate in the left column. Read across the line to the correct row spacing indicated at the top to find the number of fluid ounces per 1000 row feet that will provide the desired application rate per acre.

Fluid oz. per acre	Fluid ounces per 1000 row feet														
	Space between rows (inches)														
	12	14	16	18	20	22	24	26	28	30	32	34	36	38	40
3.75	0.09	0.10	0.11	0.13	0.14	0.16	0.17	0.19	0.20	0.22	0.23	0.24	0.26	0.27	0.29
6.50	0.15	0.17	0.20	0.22	0.25	0.27	0.30	0.32	0.35	0.37	0.40	0.42	0.45	0.47	0.50
13.00	0.30	0.35	0.40	0.45	0.50	0.55	0.60	0.65	0.70	0.75	0.80	0.85	0.90	0.95	0.99

CHEMIGATION INSTRUCTIONS

GENERAL INFORMATION:

- Apply this product through pressurized irrigation systems such as drip (trickle) irrigation (including micro-irrigation through spaghetti tubes or individual tubes) or sprinkler irrigation (including impact or microsprinklers, microjet, overhead boom, water gun, solid set, lateral move, end tow, side-roll, center pivot, or hand move, including mist-type systems); or with hand-held calibrated irrigation equipment (such as a hand-held wand with injector). Do not apply this product through any other type of irrigation system.
- Crop injury or lack of effectiveness can result from non-uniform distribution of treated water.
- If you have questions about calibration, contact State Extension Service specialists, equipment manufacturers or other experts.
- Do not connect an irrigation system (including greenhouse systems) used for pesticide application to a public water system unless the pesticide label-prescribed safety devices for public water systems are in place.
- A person knowledgeable of the chemigation system and responsible for its operation, or under the supervision of the responsible person, shall shut the system down and make necessary adjustments should the need arise.
- Public water system means a system for the provision to the public of piped water for human consumption if such system has at least 15 service connections or regularly serves an average of at least 25 individuals daily at least 60 days out of the year.
- Chemigation systems connected to public water systems must contain a functional, reduced-pressure zone, backflow preventer (RPZ) or the functional equivalent in the water supply line

upstream from the point of pesticide introduction. As an option to the RPZ, the water from the public water system should be discharged into a reservoir tank prior to pesticide introduction. There shall be a complete physical break (air gap) between the outlet end of the fill pipe and the top or overflow rim of the reservoir tank of at least twice the inside diameter of the fill pipe.

- The pesticide injection pipeline must contain a functional, automatic, quick-closing check valve to prevent the flow of fluid back toward the injection.
- The pesticide injection pipeline must contain a functional, normally closed, solenoid-operated valve located on the intake side of the injection pump and connected to the system interlock to prevent fluid from being withdrawn from the supply tank when the irrigation system is either automatically or manually shut down.
- The system must contain functional interlocking controls to automatically shut off the pesticide injection pump when the water pump motor stops, or in cases where there is no water pump, when the water pressure decreases to the point where pesticide distribution is adversely affected.
- Systems must use a metering pump, such as a positive displacement injection pump (e.g., diaphragm pump) effectively designed and constructed of materials that are compatible with pesticides and capable of being fitted with a system interlock.
- Do not apply when wind speed favors drift beyond the area intended for treatment.
- Remove scale, pesticide residues, and other foreign matter from the chemical supply tank and injector system and flush with clean water before use. Failure to provide a clean tank, free of scale or residues may reduce effectiveness of this product.

DRIP (TRICKLE) AND MICRO-IRRIGATION CHEMIGATION:

- The system must contain a functional check valve, vacuum relief valve and low pressure drain appropriately located on the irrigation pipeline to prevent water source contamination from backflow.
- The pesticide injection pipeline must contain a functional, automatic, quick-closing check valve to prevent the flow of fluid back toward the injection pump.
- The pesticide injection pipeline must also contain a functional, normally closed, solenoid-operated valve located on the intake side of the injection pump and connected to the system interlock to prevent fluid from being withdrawn from the supply tank when the irrigation system is either automatically or manually shut down.
- The system must contain functional interlocking controls to automatically shut off the pesticide injection pump when the water pump motor stops.
- The irrigation line or water pump must include a functional pressure switch which will stop the water pump motor when the water pressure decreases to the point where pesticide distribution is adversely affected.
- Systems must use a metering pump such as a positive displacement injection pump (i.e., diaphragm pump) effectively designed and constructed of materials that are compatible with pesticides and capable of being fitted with a system interlock.
- Dilute the product in water following the label mixing directions. It may be premixed in a supply tank with water, fertilizer, or other appropriate tank-mixed agricultural chemicals. Agitation is necessary. Apply to moderately moist soils. Use volumes that thoroughly wet the soil but that do not cause significant runoff or excessive drip from pots. Application should be continuous in sufficient water to apply the recommended rate evenly to the entire treated area.

SPRINKLER CHEMIGATION:

- The system must contain a functional check valve, vacuum relief valve, and low pressure drain appropriately located on the irrigation pipeline to prevent water source contamination from backflow.
- The pesticide injection pipeline must contain a functional, automatic, quick-closing check valve to prevent the flow of fluid back toward the injection pump.
- The pesticide injection pipeline must also contain a functional, normally closed, solenoid-operated valve located on the intake side of the injection pump and connected to the system interlock to prevent fluid from being withdrawn from the supply tank when the irrigation system is either automatically or manually shut down.
- The system must contain functional interlocking controls to automatically shut off the pesticide injection pump when the water pump motor stops.
- The irrigation line or water pump must include a functional pressure switch which will stop the water pump motor when the water pressure decreases to the point where pesticide distribution is adversely affected.
- Systems must use a metering pump, such as a positive displacement injection pump (i.e., diaphragm pump) effectively designed and constructed of materials that are compatible with pesticides and capable of being fitted with a system interlock.
- Dilute the product in water following the label mixing directions. It may be premixed in a supply tank with water, fertilizer or other appropriate tank-mixed agricultural chemicals. Agitation is necessary. Apply to moderately moist soils. Use volumes that thoroughly wet the soil but that do not cause significant runoff or excessive drip from pots. Application should be continuous in sufficient water to apply the recommended rate evenly to the entire treated area.
- Do not apply when wind speed favors drift beyond the area intended for treatment.

CROPS, DISEASES AND APPLICATION RATES

ARTICHOKES (Chinese and Jerusalem)		
DISEASES/PATHOGENS	**RATES**	**ADDITIONAL INFORMATION**
Gray mold/Botrytis rot (*Botrytis cinerea*) **Powdery mildew** (*Leveillula taurica, Erysiphe cichoracearum*)	3.75 - 13.0 fl. oz./acre (0.21 - 0.72 oz. a.i./acre) Do not apply more than 4.2 oz. a.i./acre/season (6 appl. at max. rate).	Begin applications at first sign of disease symptoms and repeat on 7-14 day interval as long as conditions favor disease development. Apply as a foliar spray in sufficient water to achieve thorough coverage of all above-ground plant parts. May also be applied through overhead sprinkler irrigation. See "Chemigation Instructions" for additional information.

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BERRIES AND SMALL FRUITS: **Amur river grape, Aronia berry, Bayberry, Bearberry, Bilberry, Blackberry, Blueberry, Buffalo currant, Buffaloberry, Che, Chilean Guava, Chokecherry, Cloudberry, Cranberry, Currant (red and black), Elderberry, European barberry, Gooseberry, Highbush cranberry, Honeysuckle (edible), Huckleberry, Jostaberry, Juneberry, Kiwi (fuzzy and hardy), Loganberry, Maypop, Mountain pepper berries, Mulberry, Muntries, Native currant, Partridgeberry, Phalsa, Pincherry, Raspberry (black and red), Riberry, Salal, Schisandra berry, Sea buckthorn, Serviceberry, Strawberry, Wild raspberries, Cultivars, varieties, and/or hybrids of these** (See separate table for grapes.)		
DISEASES/PATHOGENS	**RATES**	**ADDITIONAL INFORMATION**
***Alternaria* leaf spot and fruit rot** (*Alternaria* spp.) **Anthracnose leaf & fruit rot** (*Colletotrichum* spp.)* **Gray mold/fruit rot/Botrytis blight** (*Botrytis cinerea*) **Powdery mildew** (*Sphaerotheca macularis*, *Erysiphe* spp.)	3.75 - 13.0 fl. oz./acre (0.21 - 0.72 oz. a.i./acre) Do not apply more than 4.2 oz. a.i./acre/season (6 appl. at max. rate).	Apply as a foliar spray in sufficient water to provide thorough coverage. Can also be applied through overhead sprinkler irrigation. See "Chemigation Instructions" for additional information. Begin as a preventative application and continue on a 7-14 day interval as needed to maintain control. For control of *Botrytis* and other fruit diseases, begin applications at flowering.
* Suppression only. A rate of 6.5 fl. oz./acre may be used for preventative applications before onset of visible disease, in periods of low disease pressure, or in a tank mix with other fungicides for resistance management. Otherwise, use a rate of 13.0 fl. oz./acre.		

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BRASSICA (COLE) LEAFY VEGETABLES: Broccoli, Broccoli raab, Brussels Sprouts, Cabbage, Chinese broccoli, Chinese Cabbage (Bok Choi, Napa, Gai choy), Cauliflower, Cavalo broccolo, Collards, Kale, Kohlrabi, Mizuna, Mustard Greens, Mustard spinach, Rape greens		
DISEASES/PATHOGENS	**RATES**	**ADDITIONAL INFORMATION**
Alternaria leaf spot (*Alternaria* spp.) **Anthracnose** (*Colletotrichum* spp.) **Gray mold** (*Botrytis cinerea*) **White spot** (*Cercosporella* spp.)	3.75 - 13.0 fl. oz./acre (0.21 - 0.72 oz. a.i./acre) Do not apply more than 4.2 oz. a.i./acre/season (6 appl. at max. rate).	Apply as a foliar spray in sufficient water to attain thorough coverage. Use of an adjuvant may enhance spray coverage, especially of waxy leaves. Begin preventive sprays when conditions favor disease development, and continue on a 7-14 day spray interval as needed.
Bottom rot (*Rhizoctonia solani*) **Sclerotinia rot** (*Sclerotinia sclerotiorum*)		Apply in 30 - 50 gallons of water per acre as a directed spray toward soil surface and lower leaves. Begin applications at head formation, before leaves contact the ground. Repeat every 7-14 days as needed to maintain control.

BULB VEGETABLES: Chive, Daylily, Elegans hosta, Fritillaria, Garlic, Kurrat, Lady's leek, Leek, Lily, Onion, Shallot, Cultivars, varieties, and/or hybrids of these		
DISEASES/PATHOGENS	**RATES**	**ADDITIONAL INFORMATION**
Alternaria blight and Purple blotch (*Alternaria* spp.) **Botrytis leaf blight /Leaf spot/Neck rot** (*Botrytis* spp.) **Downy mildew** (*Peronospora* spp.)* **Rust** (*Puccinia alii* or *Puccinia porri*)	3.75 - 13.0 fl. oz./acre (0.21 - 0.72 oz. a.i./acre) Do not apply more than 4.2 oz. a.i./acre/season (6 appl. at max. rate).	Apply as foliar preventative spray (ground, aerial, or through overhead sprinklers) before disease onset and continue at 7-14 day intervals as needed to maintain control. Coverage may be enhanced by use of a spray adjuvant.
* Suppression only. A rate of 6.5 fl. oz./acre may be used for preventative applications before onset of visible disease, in periods of low disease pressure, or in a tank mix with other fungicides for resistance management. Otherwise, use a rate of 13.0 fl. oz./acre.		

CARROTS and PARSNIPS		
DISEASES/PATHOGENS	**RATES**	**ADDITIONAL INFORMATION**
Alternaria leaf blight (*Alternaria dauci*) **Cercospora leaf blight** (*Cercospora carotae*) **Powdery mildew** (*Erysiphe polygoni*) **Rhizoctonia crown rot and leaf blight** (*Rhizoctonia solani*)	3.75 - 13.0 fl. oz./acre (0.21 - 0.72 oz. a.i./acre) Do not apply more than 4.2 oz. a.i./acre/season (6 appl. at max. rate).	Begin applications soon after plant emergence and repeat on 7-14 day interval as long as conditions favor disease development. Apply as a foliar spray in sufficient water to achieve thorough coverage of all above-ground plant parts. May also be applied through overhead sprinkler irrigation. See "Chemigation Instructions" for additional information.

CITRUS FRUITS: **Calamondin, Citron, Citrus hybrids (Chironja, Tangelo, Tangor), Clementine, Grapefruit, Kumquat, Lemon, Lime, Mandarin (Tangerine), Orange, Pummelo, Sutsuma mandarin**		
DISEASES/PATHOGENS	**RATES**	**ADDITIONAL INFORMATION**
***Alternaria* brown spot** (*Alternaria alternata*)	3.75 - 13.0 fl. oz./acre (0.21 - 0.72 oz. a.i./acre) Do not apply more than 4.2 oz. a.i./acre/season (6 appl. at max. rate).	Apply as preventative foliar spray before disease development, when spring flush is ¼ to ½ expanded. If needed, make second application to fully expanded flush.
Botrytis rot (*Botrytis cinerea*)		Begin preventative applications during bloom when rain or fog is expected. Repeat every 7-14 days as long as conditions favoring disease persist.
Septoria spot (*Septoria citri*)		Apply as a preventative spray in late fall or early winter, just before or after the first rain. Additional applications may be necessary during seasons of heavy rainfall.

CUCURBIT VEGETABLES: **Chayote (fruit), Chinese waxgourd (Chinese preserving melon), Citron melon, Cucumber, Gherkin, Gourd (edible, including hyotan, cucuzza, hechima, Chinese okra), *Momordica* spp. (includes balsam apple, balsam pear, bitter melon, Chinese cucumber), Muskmelon (includes true cantaloupe, cantaloupe, casaba, crenshaw melon, golden pershaw melon, honeydew melon, honey balls, mango melon, Persian melon, pineapple melon, Santa Claus melon, and snake melon), Pumpkin, Squash (including acorn squash, butternut squash, calabaza, crookneck squash, hubbard squash, scallop squash, spaghetti squash, straightneck squash, vegetable marrow, zucchini), Watermelon, Hybrids and varieties of these**		
DISEASES/PATHOGENS	**RATES**	**ADDITIONAL INFORMATION**
Anthracnose (*Colletotrichum orbiculare*) **Early blight** (*Alternaria* sp.) **Gray mold** (*Botrytis* sp.) **Gummy stem blight** (*Didymella bryoniae* and *Phoma cucurbitacearum*) **Powdery mildew** (*Erysiphe* and *Sphaerotheca* spp. and *Podosphaera xanthii*) **Scab** (*Cladosporium* sp.) **Target leaf spot/Corynespora leaf spot/ Corynespora blight** (*Corynespora crassiicola*)	3.75 - 13.0 fl. oz./acre (0.21 - 0.72 oz. a.i./acre) Do not apply more than 4.2 oz. a.i./acre/season (6 appl. at max. rate).	Mix in sufficient volume of water for good spray coverage (typically 50-100 gallons per acre). Begin preventive sprays when conditions favor disease development, and continue on a 7-14 day spray interval as needed.
Southern blight (*Sclerotium rolfsii*)		See additional instructions under BANDED (IN-FURROW) APPLICATION. Can also be applied through surface (not buried) drip or overhead sprinkler irrigation. See "Chemigation Instructions" for additional information. Make subsequent applications at 7-14 day intervals either through surface drip or overhead sprinkler irrigation, or as a spray/drench directed at the base of each plant.

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FRUITING VEGETABLES: Eggplant, Groundcherry, Peppers (all types), Tomatillo, Tomatoes (all types)		
DISEASES/PATHOGENS	**RATES**	**ADDITIONAL INFORMATION**
Anthracnose (*Colletotrichum* spp.)* **Early blight** (*Alternaria solani*) **Gray mold/Botrytis rot** (*Botrytis* spp.) **Late blight*** (*Phytophthera infestans*) **Leaf mold** (*Fulvia (Cladosporium) fulvum*, also known as *Passalora fulva*) **Powdery mildew** (*Leveillula, Oidiopsis, Erysiphe*, and *Sphaerotheca* spp.)	3.75 - 13.0 fl. oz./acre (0.21 - 0.72 oz. a.i./acre) Do not apply more than 4.2 oz. a.i./acre/season (6 appl. at max. rate).	Apply as a preventative foliar spray when conditions favor disease development. Repeat application at 7-14 day intervals as needed during infection periods. Mix in sufficient water to attain thorough coverage of foliage and fruit (if present).
Southern blight (*Sclerotium rolfsii*)* **Verticillium wilt** (*Verticillium dahliae*)*		See additional instructions under BANDED (IN-FURROW) APPLICATION. Can also be applied through surface (not buried) drip or overhead sprinkler irrigation. See "Chemigation Instructions" for additional information. Make subsequent applications at 7-14 day intervals either through surface drip or overhead sprinkler irrigation, or as a spray/drench directed at the base of each plant.
* Suppression only. A rate of 6.5 fl. oz./acre may be used for preventative applications before onset of visible disease, in periods of low disease pressure, or in a tank mix with other fungicides for resistance management. Otherwise, use a rate of 13.0 fl. oz./acre.		

GINSENG		
DISEASES/PATHOGENS	**RATES**	**ADDITIONAL INFORMATION**
Alternaria blight (*Alternaria panax*) **Botrytis blight** (*Botrytis cinerea*)	3.75 - 13.0 fl. oz./acre (0.21 - 0.72 oz. a.i./acre) Do not apply more than 4.2 oz. a.i./acre/season (6 appl. at max. rate).	Apply as foliar spray every 7-10 days beginning within 2 weeks after plant emergence, prior to disease development (consult local extension service for advice on timing against these diseases). Continue throughout the season as needed to maintain control.
Cylindrocarpon root rot (*Cylindrocarpon destructans*) **Rhizoctonia root and crown rot** (*Rhizoctonia solani*)		Apply as soil drench every 14-28 days, beginning within 2 weeks after plant emergence.

GRAPES: For pre-harvest use on all grapes		
DISEASES/PATHOGENS	**RATES**	**ADDITIONAL INFORMATION**
Gray mold/bunch rot (*Botrytis cinerea*) **Powdery mildew** (*Erysiphe* (*Uncinula*) *necator*)	3.75 - 13.0 fl. oz./acre (0.21 - 0.72 oz. a.i./acre) Do not apply more than 4.2 oz. a.i./acre/season (6 appl. at max. rate).	For powdery mildew, begin as a preventative spray and repeat every 14 days as needed to maintain control. For *Botrytis* bunch rot, apply at veraison and 7 days before harvest.

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LEAFY VEGETABLES: **Amaranth, Arugula (garden rocket), Asparagus chicory, Beet greens (spinach beet), Borage, Catalogna, Celery, Chard, Chaya, Chicory, Colocasia, Corn salad (mâche), Dandelion, Endive, Escarole, Fenugreek, Garden cress, Ground-elder, Kailan, Lettuce (Head, Leaf, Iceberg, Romaine), Mizuna, Purslane, Radichetta, Radicchio, Sorrel, Spinach, Spinach beet (beet greens), Spring greens (Spring mix), Stinging nettle, Tatsoi, Tropaeolum (*Nasturtium*), Turnip greens, Watercress (*Nasturtium*), Water spinach (ong choy), Yarrow**		
DISEASES/PATHOGENS	**RATES**	**ADDITIONAL INFORMATION**
Alternaria leaf spot (*Alternaria* spp.) **Downy mildew** (*Bremia lactucae* and *Peronospora* spp.)* **Powdery mildew** (*Golovinomyces (Erysiphe) cichoracearum*)	3.75 - 13.0 fl. oz./acre (0.21 - 0.72 oz. a.i./acre) Do not apply more than 4.2 oz. a.i./acre/season (6 appl. at max. rate).	Begin applications soon after plant emergence or transplanting and repeat on 7-14 day interval as long as conditions favor disease development. Apply as a foliar spray in sufficient water to achieve thorough coverage of all above-ground plant parts. May also be applied through overhead sprinkler irrigation. See "Chemigation Instructions" for additional information.
Botrytis damping off (*Botrytis* spp.)		Apply as banded spray (4-6" wide) over the seed furrow at planting or transplanting. See additional instructions under BANDED (IN-FURROW) APPLICATION.
Botrytis leaf blight, Botrytis rot (*Botrytis* spp.)		Begin preventative foliar applications when conditions favor disease development and continue at 7-14 day intervals as long as needed to maintain control.
Bottom rot (*Rhizoctonia solani*)		Apply in 30 - 50 gallons of water per acre as a directed spray toward soil surface and lower leaves. Begin applications at head formation, before leaves contact the ground. Repeat every 7-14 days as needed to maintain control.
Lettuce drop (*Sclerotinia* spp.)		Apply in 30 - 50 gallons of water per acre as a directed spray toward soil surface and lower leaves. Make first application to direct-seeded lettuce immediately after emergence. For transplanted lettuce, make first application immediately after transplanting. In both cases, apply prior to disease development. Apply again if soil is disturbed by cultivation or thinning and conditions continue to favor disease development.
* Suppression only. A rate of 6.5 fl. oz./acre may be used for preventative applications before onset of visible disease, in periods of low disease pressure, or in a tank mix with other fungicides for resistance management. Otherwise, use a rate of 13.0 fl. oz./acre.		

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LEGUME VEGETABLES: **Bean (Lupines spp.), Bean (*Phaseolus* spp., including Field bean, Kidney bean, Lima bean, Navy bean, Pinto bean, Runner bean, Snap bean, Tepary bean, Wax bean), Bean (*Vigna* spp., including Adzuki bean, Asparagus bean, Blackeyed pea, Catjang, Chinese longbean, Cowpea, Crowder pea, Moth bean, Mung bean, Southern pea, Urd bean, Yardlong bean) Broad bean (Fava bean), Chickpea (Garbanzo bean), Guar, Jackbean, Lablab bean (hyacinth bean), Lentil, Pea (*Pisum* spp., including Dwarf pea, Edible pod pea, English pea, Field pea, Garden pea, Green pea, Snow pea, Sugar snap pea), Pigeon pea, Soybean, Sward bean.**		
DISEASES/PATHOGENS	**RATES**	**ADDITIONAL INFORMATION**
Asian Soybean Rust (*Phakopsora pachyrhizi*) **Gray mold** (*Botrytis cinerea*) **Powdery mildew** (*Erysiphe pisi*)	3.75 - 13.0 fl. oz./acre (0.21 - 0.72 oz. a.i./acre) Do not apply more than 4.2 oz. a.i./acre/season (6 appl. at max. rate).	Begin applications at first sign of disease symptoms and repeat on 7-14 day interval as long as conditions favor disease development. Apply as a foliar spray in sufficient water to achieve thorough coverage of all above-ground plant parts. May also be applied through overhead sprinkler irrigation. See "Chemigation Instructions" for additional information.
Stem rot / White mold (*Sclerotinia sclerotiorum*)		Apply in 30 - 50 gallons of water per acre as a directed spray toward soil surface, lower leaves, and stems. May also be applied through overhead sprinkler irrigation. See "Chemigation Instructions" for additional information.

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POME FRUITS: Apple, Crabapple, Loquat, Mayhaw, Pear, Quince		
DISEASES/PATHOGENS	**RATES**	**ADDITIONAL INFORMATION**
Alternaria leaf spot (*Alternaria mali*) **Leaf blotch** (*Diplocarpon mali*) **Powdery mildew** (*Podosphaera leucotricha, Phyllactinia mali*) **Scab** (*Venturia* spp.)*	3.75 - 13.0 fl. oz./acre (0.21 - 0.72 oz. a.i./acre) Do not apply more than 4.2 oz. a.i./acre/season (6 appl. at max. rate).	Apply as foliar spray in sufficient water to attain thorough coverage of foliage and fruit. For powdery mildew control, begin as preventative and repeat on 7-14 day interval as needed. Use in an alternating program with a sterol inhibitor (DMI) fungicide. For scab suppression, begin sprays at green tip and continue every 7-10 days as needed.
* Suppression only. A rate of 6.5 fl. oz./acre may be used for preventative applications before onset of visible disease, in periods of low disease pressure, or in a tank mix with other fungicides for resistance management. Otherwise, use a rate of 13.0 fl. oz./acre.		

POTATOES		
DISEASES/PATHOGENS	**RATES**	**ADDITIONAL INFORMATION**
Black scurf (*Rhizoctonia solani*)	3.75 - 13.0 fl. oz./acre (0.21 - 0.72 oz. a.i./acre) Do not apply more than 4.2 oz. a.i./acre/season (6 appl. at max. rate).	Apply as banded spray in-furrow at planting, either just before placement of seed pieces or over seed pieces before covering with soil. See additional instructions under BANDED (IN-FURROW) APPLICATION.
Early blight (*Alternaria solani*) **Late blight** (*Phytophthora infestans*)*		Apply as a foliar spray in sufficient water to provide thorough coverage of all foliage. May also be applied through overhead sprinkler irrigation. See "Chemigation Instructions" for additional information. Begin as a preventative application and continue on a 7-14 day interval as needed to maintain control.
White mold (*Sclerotinia sclerotiorum*)		Apply in 30 - 50 gallons of water per acre as a directed spray toward soil surface, lower leaves, and stems. May also be applied through overhead sprinkler irrigation. See "Chemigation Instructions" for additional information.
* Suppression only. A rate of 6.5 fl. oz./acre may be used for preventative applications before onset of visible disease, in periods of low disease pressure, or in a tank mix with other fungicides for resistance management. Otherwise, use a rate of 13.0 fl. oz./acre.		

STONE FRUITS: Apricot, Cherry, Nectarine, Peach, Plum, Plumcot, Prune (fresh), and hybrids		
DISEASES/PATHOGENS	**RATES**	**ADDITIONAL INFORMATION**
Botrytis blossom blight (*Botrytis cinerea*) **Powdery mildew** (*Podosphaera* spp., *Sphaerotheca pannosa*)	3.75 - 13.0 fl. oz./acre (0.21 - 0.72 oz. a.i./acre) Do not apply more than 4.2 oz. a.i./acre/season (6 appl. at max. rate).	Apply as foliar spray in sufficient water to attain thorough coverage of foliage and fruit. For powdery mildew control, begin as preventative and repeat on 7-14 day interval as needed. Use in an alternating program with a sterol inhibitor (DMI) fungicide. Apply at full bloom for control of *Botrytis* blossom blight if wet weather occurs during bloom.

SUGAR BEET		
DISEASES/PATHOGENS	**RATES**	**ADDITIONAL INFORMATION**
Cercospora leaf spot (*Cercospora beticola*)	3.75 - 13.0 fl. oz./acre (0.21 - 0.72 oz. a.i./acre) Do not apply more than 4.2 oz. a.i./acre/season (6 appl. at max. rate).	Begin applications at first sign of disease symptoms and repeat on 7-14 day interval as long as conditions favor disease development. Apply as a foliar spray in sufficient water to achieve thorough coverage of all above- ground plant parts. May also be applied through overhead sprinkler irrigation. See "Chemigation Instructions" for additional information.
Rhizoctonia crown and root rot (*Rhizoctonia solani*)		Apply as banded spray or drench in seed furrow at planting. See additional instructions below for banded application rates. Can also be applied through overhead sprinkler irrigation. See "Chemigation Instructions" for additional information. Make subsequent applications at 7-14 day intervals either through chemigation, or as a spray/drench directed at the base of each plant.

068173-0000U.20120927.Changes_IMPLEMENTED.pdf
VEGGIETURBO 5SC (EPA File Symbol 68173-U) • Page 19 of 19
September 27, 2012 Revised Proposed Master Label
Updates the September 20, 2012 proposed label directions for use tables.
Changes IMPLEMENTED

STORAGE AND DISPOSAL

Do not contaminate water, food or feed by storage or disposal.
PESTICIDE STORAGE: Store in dry place away from food or feed.
PESTICIDE DISPOSAL: Wastes resulting from the use of this product may be disposed of on site or at an approved waste disposal facility.
CONTAINER HANDLING: Nonrefillable container. Do not reuse or refill this container. Completely empty container into application equipment. Triple rinse (or equivalent). Then offer for recycling or reconditioning (if available), or puncture and dispose of in a sanitary landfill or by incineration, if allowed by State and local authorities. If burned, stay out of smoke.

WARRANTY

Kaken Pharmaceutical Co., Ltd. warrants that the material contained herein conforms to the description on the label and is reasonably fit for the purpose referred to in the directions for use. Timing and method of application, weather, watering practices, nature of soil, the disease problem, condition of the crop, incompatibility with other influencing factors in the use of this product are beyond the control of the seller. Buyer assumes all risks of use, storage, or handling of this material not in strict accordance with directions given herein. TO THE EXTENT CONSISTENT WITH APPLICABLE LAW, NO OTHER EXPRESSED OR IMPLIED WARRANTY OF THE FITNESS OR MERCHANTABILITY IS MADE.

VEGGIETURBO™ is a trademark of Kaken Pharmaceutical Co., Ltd.

Label Version No. _____

EPA review of the data submitted to support the expanded tolerance exemption for polyoxin D zinc salt and associated amendment of the registration for Polyoxin D Zinc Salt Technical

Polyoxin D zinc salt (PC 230000)
EPA Reg. No.: 68173-1

DP Number: 397074

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

WASHINGTON, D.C. 20460

OFFICE OF PREVENTION, PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

DATE: May 11, 2012

SUBJECT: Polyoxin D zinc salt (EPA Reg. #: 68173-1), Containing 23.8% of polyoxin D zinc salt (Active Ingredient). Science Review of Product Chemistry, Residue Chemistry, Non-Target Organism and Toxicity Data in Support of label Amendment

Decision Number: 457591
DP Number: 397074
EPA Symbol #: 68173-1
Chemical Class: Biochemical
PC Code: 230000
MRIDs: 48653302-48653307; 48653313-48653315; 48660403 & 48660404

From: Manying Xue, Chemist
BPB/BPPD (7511P)

To: Colin Walsh, Regulatory Action Leader
BPB/BPPD (7511P)

Action Requested:

Karen Pharmaceutical Co., Ltd. has submitted a petition for exemption from the requirement of a tolerance for residues of Polyoxin D zinc salt (EPA Reg. #: 68173-1). Karen Pharmaceutical Co., Ltd. has proposed to expand the exemption to all agricultural commodities.

In support of this petition, the registrant had submitted data for product chemistry, label, toxicity, residue chemistry, and proposed tolerances, etc..

An exemption from the requirement of a tolerance has been established on 40 CFR 180.1285 for the residues of the biochemical pesticide polyoxin D zinc salt when used as a fungicide on almonds, cucurbit vegetables, fruiting vegetables, ginseng, grapes, pistachios, pome fruits, potatoes and strawberries.

BPPD has examined the submitted data for product chemistry, label, toxicity, residue chemistry, and proposed tolerances, etc. for Polyoxin D zinc salt (EPA EPA #: 68173-1). The decisions are made to reflect the current OCSPP's policies.

Recommendations and Conclusions:

1. The submitted scientific data of product chemistry, toxicity, non-target organism and Insect Testing, etc. support the petition for expanding exemption from the requirement of a tolerance the residues of the biochemical pesticide polyoxin D zinc salt in all agriculture commodities.

2a. The submitted nature of residue study is **ACCEPTABLE**. The TRR level in fruit from grape plant treated with [^{14}C]Polyoxin D (three applications at a rate of 1.67 times of 150 g a.i./ha) was 0.520 ppm at Day 1, 0.538 ppm at Day 14 and 0.495 ppm at Day 30 after the final application; total radioactive residues (TRR) were 3.078 ppm detected in the tomato fruits from tomato plants treated with Polyoxin D at 28, 21, and 14 days before final harvest at the rate of 100 grams a.i./ha per application; the TRR in the head (edible part) from the lettuce plant treated with [^{14}C]Polyoxin D at the rate of 300 g a.i./ha was low: 0.025 ppm and 0.107 ppm at Day-7 and Day-14, respectively.

2b. The major metabolic pathway of Polyoxin D in grape plant was formation of uracil-5-carboxylic acid. This metabolite was further metabolized and considered to be incorporated into plant constituents of pectin, lignin and hemi-cellulose etc. followed by formation of bound residues.

2c. The metabolism of Polyoxin D in tomato involved cleavage of the pyrimidinyl linkage to produce uracil-5-carboxylic acid. These results are consistent with those obtained from other Polyoxin D plant metabolism studies, including experiments with grape and lettuce. A metabolic pathway is proposed based on metabolites identified.

2d. The major metabolic pathway of Polyoxin D in lettuce plant was formation of uracil-5-carboxylic acid. This metabolite was considered to be further metabolized into various polar metabolites followed by formation of bound residues.

3. The waiver request for nature of the residue study in livestock is **ACCEPTABLE.**

4. The submitted waiver requests for all residue chemistry data requirements are **ACCEPTABLE**.

5. The photolysis study is **ACCEPTABLE**. The photolytic degradation of [^{14}C]Polyoxin D was analyzed in an 11-day study in sterile buffers at pH 5.0, pH 7.0, pH 9.0, and sterile natural water. The net photolytic half-lives of [^{14}C]Polyoxin D were calculated to be 0.4 days, 4 days, 2.4 days, and 1.6 days in sterile natural water, pH 5.0, pH 7.0, and pH 9.0 buffers, respectively.

6. The hydrolysis study is **ACCEPTABLE**. The hydrolysis of [^{14}C]Polyoxin D was analyzed in a 30-day study in sterile buffers at pH 4.0, pH 5.0, pH 7.0 and pH 9.0. The half-lives of [^{14}C]Polyoxin D were calculated to be 301.3 days, 231.0, 32.5 and 9.1 days in sterile pH 4.0, pH 5.0, pH 7.0 and pH 9.0 buffers, respectively.

7. The study of UV/Visible Absorption is **ACCEPTABLE.** The UV absorbance of Polyoxin D Zinc Salt in neutral, acidic and basic solutions was 270.0 nm, 274.0 nm and 268.5 nm, respectively.

8. The developmental toxicity study in the rat is classified **ACCEPTABLE** and satisfies the guideline requirement for a developmental toxicity study (OCSPP 870.3700; OECD 414) in the rat. The developmental toxicity LOAEL for Polyoxin D zinc salt is not determined. The NOAEL is ≥1000 mg/kg bw/day.

9. The submitted gene mutation assay is **ACCEPTABLE.** There was no evidence of cytotoxicity or insolubility. Acceptable experimental protocols were followed, and solvent and positive control values were appropriate for the respective strains. The test article did not increase the mean number of revertants per plate by a factor of two or more over the corresponding solvent control values for any of the five strains tested at any of the tested concentrations, without or with S9-mix. None of the experimental numbers of revertant colonies even approached a number that would suggest a biologically significant positive result, even at the limiting dose of 5000 µg/plate.

10. The submitted cell cytogenetics assay is classified as **ACCEPTABLE** and satisfies the guideline requirement for Test Guideline OCSPP 870.5375 [*In vitro* mammalian chromosome aberration test; OECD 473] for *in vitro* cytogenetic mutagenicity data.

11. The submitted study for insect testing is **ACCEPTABLE.** Polyoxin D zinc salt was toxic to honeybees, with 8% mortality after 96 hr. The 96-hr LD_{50} was 28.77µg/bee.

12. The submitted study of Algal Toxicity (OCSPP 850.5400) is **ACCEPTABLE.** Based on the results, the E_bC_{50} (0-72 hr) was 6.47 mg/L (95% CI = 6.31-6.63 mg/L), and the $NOEC_b$ (0-72 hr) was 5 mg/L. Based on growth rate data, the E_rC_{50} (24-48 hr) was 7.19 mg/L (95% CI = 6.94-7.47 mg/L), and the NOEC was 5 mg/L; and the E_rC_{50} (24-72 hr) was 7.05 mg/L (95% CI = 6.84-7.28 mg/L), and the NOEC was 5 mg/L.

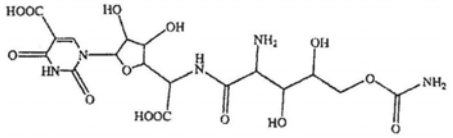
Background Information and Study Summaries

Polyoxin D and its zinc salt is the inhibition of chitin synthesis in the cell walls of fungi, some of which are pathogenic to plants. This inhibition of chitin synthesis is limited to chitin in fungal cell walls. 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. Polyoxin D Zinc Salt does not affect mammals because mammalian cells have plasma membranes that do not contain chitin.

Polyoxin D Zinc Salt is used exclusively on plants as an anti-fungal agent in the United States and elsewhere. Based upon maximum inhibitory concentration (MIC) evaluations, Polyoxin D Zinc Salt is not effective as an anti-bacterial agent. Polyoxin D Zinc Salt has never been used as an antibiotic in human or veterinary medicine. Polyoxin D Zinc Salt is not effective in inhibiting bacteria and yeast, but in the 14 fungal species tested,

effectiveness of inhibition ranged from highly effective to ineffective. The chemical structure and chemical names of Polyoxin D Zinc Salt are provided (MRID 48653307) in Table 1.

Table1. Test Compound Nomenclature.

Compound	 Chemical Structure
Common name	Polyoxin D Zinc Salt
Company experimental name	Polyoxin D Zinc Salt
IUPAC name	5-(2-amino-5-*O*-carbamoyl-2-deoxy-L-xylonamido)-5-deoxy-1-(1,2,3,4-tetrahydro-5-carboxy-2,4-dioxopyrimidinyl)-ß-D-allofuranuronic acid
CAS name	β-D-allofuranuronic acid, 5-[[2-amino-5-*O*-(aminocarbonyl)-2-deoxy-L-xylonyl]amino]-1-(5-carboxy-3,4-dihydro-2,4-dioxo-1(2*H*)-pyrimidinyl)-1,5-dideoxy-, zinc salt (1:1)
CAS registry number	146659-78-1
Use product	Polyoxin D Zinc Salt Technical

860.1200 Directions for Use (MRID 48653307)

Polyoxin D Zinc Salt is applied as a foliar spray to food crops, turf and ornamentals to control and/or suppress fungal diseases. Registered food uses were summarized for the United States and internationally. In the United States maximum use rates range from 2.1 to 4.2 oz active ingredient/acre/season, with a minimum pre-harvest interval of 0 days for all crops except ginseng, for which it is 365 days. Information was summarized for this chemical in the United States regarding EPA registration numbers, primary brand names, and application rates per application and per season. Information was also summarized for this chemical in international usage regarding countries, brand names, application rates per application and per season, and pre-harvest intervals.

It is acknowledged that if the proposed tolerance exemption for all crops is approved, the application rates in the United States might increase and the maximum number of applications per season might increase. However, such increases are unlikely to result in much increase in exposure to humans from residues of this fungicide because of the considerable expense of its production and because growers are advised to not make consecutive applications of fungicides with the same mode of action to avoid development of resistance. The mode of action of Polyoxin D and its zinc salt is the inhibition of chitin synthesis in the cell walls of fungi, some of which are pathogenic to plants. Polyoxin D and its zinc salt do not inhibit the synthesis of chitin in animals that contain chitin, and it does not affect mammals because mammalian cells have plasma

membranes that do not contain chitin. Polyoxin D Zinc Salt is used exclusively on plants as an anti-fungal agent in the United States and elsewhere. It is not effective as an anti-bacterial agent, and it has never been used as an antibiotic in human or veterinary medicine. The data reported on minimum inhibitory concentrations in numerous species of bacteria, yeast, and fungi demonstrated no effectiveness in inhibiting bacteria and yeast, but in the 14 fungal species tested, effectiveness of inhibition ranged from highly effective to ineffective.

In tests on 14 bacterial species (10 aerobic, 3 anaerobic, and 1 acid-fast), there was no demonstrated inhibition of bacterial growth in agar at concentrations up to 400 µg/mL (MRID 48653308). The species tested included pathogenic, intestinal, and other general bacteria that exist widely in nature. As expected, because bacteria contain no chitin, polyoxin D appears to have no effect on bacterial growth.

Nature of the Residue— Plants (OCSPP 860.1300)

The test substance in the study was ^{14}C-radiolabeled Polyoxin D ([^{14}C]Polyoxin D), which was radiolabeled on the second carbon of the pyrimidine ring. The specific radioactivity was 55 mCi/mmole (225.662 dpm/ µg), and the radiopurity was 97.50 %. The test substance was isotopically diluted to a calculated specific activity of 94,733 dpm/µg before it was applied to tomatoes.

Three residue trials on grapes (MRID 48653309), tomatoes (MRID 48653310), and head lettuce (MRID 48653311) in greenhouses were conducted. The application rate on grapes was 1.5 µg/cm^2 x 1.67 = 2.5 µg/cm^2, 100 g a.i./ha = 1 µg/cm^2 on tomatoes, and 300 g a.i./ha = 3 µg/cm^2 on head lettuce.

Results

The total radioactive residue (TRR) levels in fruit from grape plants treated with [^{14}C]Polyoxin D (three applications at a rate of 1.67 times the recommended rate of 150 g a.i./ha) were 0.520, 0.538, and 0.495 mg eq./kg in samples collected on days 1, 14, and 30 after the final application. The TRR level in leaves from those grape plants was 20.690 mg eq./kg in samples collected 30 days after the final application.

Low levels of TRRs were detected in ripe tomatoes harvested from tomato plants treated with [^{14}C]Polyoxin D at 28, 21, and 14 days before final harvest at the rate of 100 grams a.i./ha per application. By far most of the radioactivity in the tomato fruit was detected in the surface wash residues. Only a small percentage of the radioactivity was present in the juice (6.9% TRR) and pomace (5.4% TRR). Polyoxin D was the major residue present and was detected on the fruit surface only. No Polyoxin D was associated with the juice or pomace fraction. Uracil-5-carboxylic acid was present at 9.3% TRR. A number of minor ^{14}C residues in the mature fruit were present, none exceeding 3.3% of the TRR. The TRRs in the tomato foliage were 3.078 ppm. The major ^{14}C residues identified from the foliage included Polyoxin D and Uracil-5-carboxylic acid. The study demonstrated that Polyoxin D was readily removed from the surface of the fruit. Because only a small

percentage of the recovered radioactivity was detected in the fruit juice or pomace, there was clearly slow, or lack, of penetration of test material into the fruit. Any radioactivity that entered the fruit was extensively metabolized.

The TRR in the head (edible part) from the lettuce plant treated with [^{14}C]Polyoxin D at the rate of 300 g a.i./ha was low: 0.025 mg eq./kg and 0.107 mg eq./kg in samples collected 7 and 14 days after the last treatment. On those same days, the TRRs in the outer (wrapper) leaves from the lettuce head were 2.491 mg eq./kg and 1.890 mg eq./kg, respectively. In the studies on all three dissimilar crops, recoveries of spiked samples were acceptable and storage stability studies showed reasonable agreement between initial HPLC chromatographic profiles and HPLC chromatographic profiles taken after periods of frozen storage comparable to those occurring in the studies. Based on the results, it is appears that the major metabolic pathway of Polyoxin D in grapes, tomatoes, and head lettuce involves cleavage of the pyrimidinyl linkage to produce Uracil-5-carboxylic acid. This metabolite is then further metabolized and incorporated into plant constituents such as pectin, lignin and hemicellulose, followed by formation of bound residues.

Table 2 shows that the major radioactive components in the fruit and leaves (including both the surface rinse and extract) were unchanged [^{14}C]Polyoxin D and [^{14}C]Uracil-5-carboxylic acid.

Table 2. Measured primary radioactive residues in unwashed fruit and leaves of grape plants sprayed with [^{14}C]Polyoxin D

	Measured residues in mg eq./kg[a] (% TRR[b])			
	Fruit			Leaves
Primary radioactive residues	Day 1 ALT[c]	Day 14 ALT	Day 30 ALT	Day 30 ALT
Polyoxin D	0.3645 (69.90%)	0.2077 (39.40%)	0.1333 (26.88%)	2.5511 (12.70%)
Uracil-5-carboxylic acid	0.0339 (6.47%)	0.0621 (11.59%)	0.0673 (13.62%)	3.4666 (16.81%)
Total Identified	0.3984 (76.37%)	0.2698 (50.99%)	0.2006 (40.50%)	6.0177 (29.51%)
TRR	0.5201 (100.00%)	0.5375 (100.00)	0.4953 (100.00%)	20.6902 (100.00%)

Data copied from Table 11 on p. 74, MRID 48653309.
[a]mg eq./kg = [^{14}C]Polyoxin D equivalent concentration, that is, the radioactivity in a one kilogram of fresh plant sample when divided by the specific radioactivity of [^{14}C]Polyoxin D.
[b]% of total radioactive residues
[c]ALT = After Last Treatment

Tables 3 and 4, which show the major radioactive components in the fruit and leaves of treated tomatoes, make it clear that the major residues were unchanged [^{14}C]Polyoxin D and [^{14}C]Uracil-5-carboxylic acid.

Table 3. Measured primary radioactive residues in unwashed fruit of tomato plants sprayed with [^{14}C]Polyoxin D and collected 14 days after the last treatment

	Measured residues in ppm[a] (% TRR[b])			
Primary radioactive residues	Surface wash	Juice	Pomace	Total
Polyoxin D	0.073 (70.9%)	ND[c]	ND	0.073 (70.9%)
Uracil-5-carboxylic acid	0.005 (4.8%)	0.003 (2.5%)	0.002 (2.0%)	0.010 (9.3%)

Identified/characterized	0.078 (75.7%)	0.003 (2.5%)	0.002 (2.0%)	0.083 (80.2%)

Data copied from Table 8, p. 66 and second table, p. 15, MRID 48653310.
[a]ppm = parts per million polyoxin D equivalents determined using Liquid Scintillation Counting analysis of the liquid fractions and combustion analysis of extracted solids.
[b]% of total radioactive residues; [c]ND = not detected

Table 4. Measured primary radioactive residues in foliage extracts of tomato plants sprayed with [^{14}C]Polyoxin D and collected 14 days after the last treatment

	Measured residues in ppm[a] (% TRR[b])		
Primary radioactive residues	Water wash of homogenate	Water extract	Total
Polyoxin D	1.606 (52.2%)	0.336 (10.9%)	1.942 (63.1%)
Uracil-5-carboxylic acid	0.227 (7.4%)	0.013 (0.4%)	0.240 (7.8%)
Identified/characterized	1.833 (59.6%)	0.349 (11.3%)	2.181 (70.9%)

Data copied from Table 9, p. 67 and second table, p. 16, MRID 48653310.
[a]ppm = parts per million polyoxin D equivalents determined using Liquid Scintillation Counting analysis of the liquid fractions and combustion analysis of extracted solids.
[b]% of total radioactive residues

Tables 5 and 6 show the major radioactive components in head lettuce harvested 7 and 14 days after the final treatment, respectively. In the surface rinse of the outer (wrapper) leaves, the major residues were unchanged [^{14}C]Polyoxin D and [^{14}C]Uracil-5-carboxylic acid. At neither time of harvest was [^{14}C]Polyoxin D detected in the extract of the outer leaves or in the extract of the lettuce head; however, [^{14}C]Uracil-5-carboxylic acid was detected in both of those samples, albeit at very low levels.

Table 5. Measured primary radioactive residues in head lettuce plants harvested 7 days after last treatment with [^{14}C]Polyoxin D

	Measured residues in mg eq./kg[a] (% TRR[b])				
Primary radioactive residues	Surface Rinse of Outer Leaves	Extract of Outer Leaves	Total for Outer Leaves	Extract of Lettuce Head	Grand Total
Polyoxin D	0.7456 (29.64%)	ND[c]	0.7456 (29.64%)	ND	0.7456 (29.64%)
Uracil-5-carboxylic acid	0.3910 (15.54%)	0.0797 (3.17%)	0.4707 (18.71%)	0.0021 (0.09%)	0.4728 (18.79%)
Total identified	1.1366 (45.18%)	0.0797 (3.17%)	1.2163 (48.35%)	0.0021 (0.09%)	1.2184 (48.43%)

Data copied from Table 7A on p. 56, MRID 48653311.
Data are the mean of duplicate experiments except for the surface rinse fraction.
[a]mg eq./kg = [^{14}C]Polyoxin D equivalent concentration, that is, the radioactivity in a one kilogram of fresh plant sample when divided by the specific radioactivity of [^{14}C]Polyoxin D.
[b]% of total radioactive residues; [c]ND = not detected

Table 6. Measured primary radioactive residues in head lettuce plants harvested 14 days after last treatment with [^{14}C]Polyoxin D

	Measured residues in mg eq./kg[a] (% TRR[b])				
Primary radioactive Residues	Surface Rinse of Outer Leaves	Extract of Outer Leaves	Total for Outer Leaves	Extract of Lettuce Head	Grand Total
Polyoxin D	0.3748 (18.77%)	ND[c]	0.3748 (18.77%)	ND	0.3748 (18.77%)
Uracil-5-carboxylic acid	0.3826 (19.16%)	0.0623 (3.12%)	0.4449 (22.28%)	0.0273 (1.37%)	0.4721 (23.65%)
Total	0.7574 (37.93%)	0.0623 (3.12%)	0.8197 (41.05%)	0.0273 (1.37%)	0.8469 (42.42%)

Polyoxin D zinc salt (PC 230000) DP Number: 397074
EPA Reg. No.: 68173-1

Data copied from MRID 48653311.
Data are the mean of duplicate experiments except for the surface rinse fraction.
[a]mg eq./kg = [^{14}C]Polyoxin D equivalent concentration, that is, the radioactivity in a one kilogram of fresh plant sample when divided by the specific radioactivity of [^{14}C]Polyoxin D.
[b]% of total radioactive residues; [c]ND = not detected

Based on the metabolism studies, the proposed metabolic pathway in these three dissimilar plants is as follows:

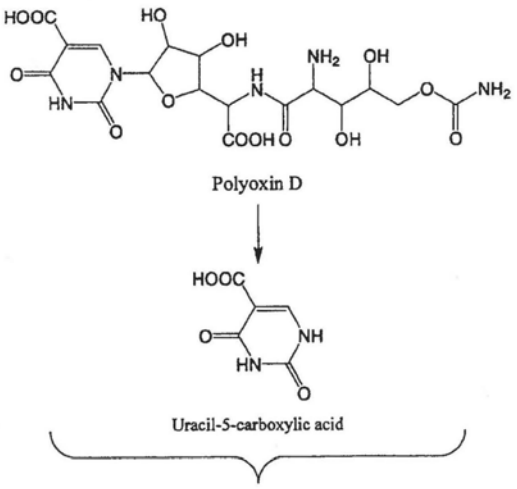


Figure copied from Fig. 10. p. 59, MRID 48653307

Conclusions:

The submitted nature of residue study is **ACCEPTABLE**. The TRR level in fruit from grape plant treated with [^{14}C]Polyoxin D (three applications at a rate of 1.67 times of 150 g a.i./ha) was 0.520 ppm at Day 1, 0.538 ppm at Day 14 and 0.495 ppm at Day 30 after the final application; total radioactive residues (TRR) were 3.078 ppm detected in the tomato fruits from tomato plants treated with Polyoxin D at 28, 21, and 14 days before final harvest at the rate of 100 grams a.i./ha per application; the TRR in the head (edible part) from the lettuce plant treated with [^{14}C]Polyoxin D at the rate of 300 g a.i./ha was low: 0.025 ppm and 0.107 ppm at Day-7 and Day-14, respectively.

The major metabolic pathway of Polyoxin D in grape plant was formation of uracil-5-carboxylic acid. This metabolite was further metabolized and considered to be incorporated into plant constituents of pectin, lignin and hemi-cellulose etc. followed by formation of bound residues.

The metabolism of Polyoxin D in tomato involved cleavage of the pyrimidinyl linkage to produce uracil-5-carboxylic acid. These results are consistent with those obtained from

other Polyoxin D plant metabolism studies, including experiments with grape and lettuce. A metabolic pathway is proposed based on metabolites identified.

The major metabolic pathway of Polyoxin D in lettuce plant was formation of uracil-5-carboxylic acid. This metabolite was considered to be further metabolized into various polar metabolites followed by formation of bound residues.

Nature of the Residue--Livestock

No nature of the residue study has been conducted in livestock. Kaken Pharmaceutical Co. Ltd. requests a waiver of the requirement for data regarding the nature of the residue in livestock based upon the available data. It was demonstrated that residues levels in crops grown in greenhouses were low and that rinsing of the raw agricultural commodities with water significantly reduced those residue levels. As a result, no significant residues would be anticipated in or on livestock feed. Based on the environmental fate data, there will be significant degradation of residues under field conditions, that is, at pH 5.0, 7.0, and 9.0, Polyoxin D undergoes rapid aqueous photolysis; at pH 7.0 and 9.0, Polyoxin D undergoes rapid hydrolysis, and Polyoxin D degrades rapidly in the soil under aerobic conditions. Also, based on environmental fate data, the route of environmental degradation is consistent with the route of crop metabolism, that is, Polyoxin is degraded to Uracil-5-carboxylic acid and several smaller metabolites, each at levels below those requiring identification. Any residues of Polyoxin D ingested by livestock should be readily eliminated in urine, based on the Polyoxin D's physical properties. Based on the carbohydrate-like structure of Polyoxin D and the crop metabolism data, it is also anticipated that Polyoxin D will be metabolized in ruminants and poultry to Uracil-5-carboxylic acid and a large number of small minor metabolites that would be used in the carbon pool for the building of ruminant and poultry body tissues.

Conclusion:

The waiver request for nature of the residue study in livestock is **ACCEPTABLE.**

Residue Analytical Method (OCSPP 860.1340)

No residue analytical method has been submitted with this petition. However, an acceptable explanation has been submitted by the registrant: "a residue analytical method suitable for the enforcement of the tolerance is not required because a numerical tolerance is not proposed. Instead, a tolerance exemption for all agricultural commodities is proposed."

Multiresidue Method (OCSPP 860.1360)

No mutiresidue method has been submitted with this petition. However, an acceptable explanation has been submitted by the registrant: "a multiresidue try-out is not required

because a numerical tolerance is not proposed. Instead, a tolerance exemption for all agricultural commodities is proposed."

Food Handling (OCSPP 860.1460)

No food handling data has been submitted with this petition. However, an acceptable explanation has been submitted by the registrant: "no uses of the fungicide polyoxin D Zinc Salt in food handling establishments are registered, proposed, or even contemplated".

Meat/Milk/Poultry/Eggs (OCSPP 860.1480)

No data for meat/milk/poultry/eggs has been submitted with this petition. However, an acceptable explanation has been submitted by the registrant: "based upon available crop metabolism and environmental fate data, no significant residues of Polyoxin D Zinc Salt are anticipated to be in meat, milk, poultry, and eggs. In addition, it was noted that because polyoxin D Zinc Salt is a polar compound with high water solubility, it should be excreted readily in the urine whenever it is ingested by livestock".

Crop Field Trials (OCSPP 860.1500)

No field trial study has been submitted with this petition. However, the registrant has analyzed data from 1) the nature of the residue data collected on grapes, tomatoes, and head lettuce grown in greenhouses (including metabolism data); 2) environmental fate data, and 3) expectations regarding the directions for use. The registrant concluded that"Greenhouse–grown and field-grown raw agricultural commodities treated with polyoxin D zinc salt are anticipated to have low residues. Residues can be easily and significantly reduced by rinsing the raw agricultural commodities with water." The conclusions are **ACCEPTALE.**

Processed Food/Feed (OCSPP 860.1520)

No processing study has been submitted with this petition. However, Kaken Pharmaceutical Co. Ltd. has submitted an acceptable waiver request regarding the magnitude of residue in processed food and feed because (1) crop metabolism and environmental fate data show that the magnitude of the residues of Polyoxin D Zinc Salt in RACs should be low, (2) food processing generally begins with a water rinse of the RAC, and crop metabolism data show that rinsing of the RAC removes a significant amount of the residue, and (3) the low levels of bound residues demonstrated are likely to be small molecules produced by catabolism that have been incorporated into natural constituents of the plants themselves such as pectin, lignin, and hemicellulose.

Anticipated Residues (OCSPP 860.1540)

No data for anticipated residue has been submitted with this petition. However, an acceptable explanation has been submitted by the registrant: "as noted in the crop

metabolism studies, significant reduction results from rinsing raw agricultural commodities with water. Therefore, through the normal rinsing of raw fruits and vegetables before consumption, residues of polyoxin D in raw agricultural commodities are anticipated to be less at the point of consumption than at the farm gate. Polyoxin D readily hydrolyzes. Therefore, cooking of raw agricultural commodities will further reduce polyoxin D residues prior to consumption of the treated commodities."

Hydrolysis (OCSPP 835.2120)

The hydrolysis study (MRID 48653304) is **ACCEPTABLE**. The hydrolysis of [^{14}C]Polyoxin D was analyzed in a 30-day study in sterile buffers at pH 4.0, pH 5.0, pH 7.0 and pH 9.0. At intervals during incubation, aliquots were collected from each sample and analyzed directly by high-performance liquid chromatography with radiochemical flow detection (HPLC-RAD) to determine the distribution of radioactivity and identification of degradation products. At 25 ± 0.1°C, Polyoxin D hydrolyzes very rapidly at pH 9.0 and pH 7.0 and hydrolyzes at a slow rate at pH 4.0 and pH 5.0. The half-lives of [^{14}C]Polyoxin D were calculated to be 301.3 days, 231.0, 32.5 and 9.1 days in sterile pH 4.0, pH 5.0, pH 7.0 and pH 9.0 buffers, respectively.

The hydrolysis product observed at pH 4.0, pH 5.0, pH 7.0 and pH 9.0 was formed by cleavage of the pyrimidinyl linkage to produce the corresponding uracil-5-carboxylic acid probably via Polyoxin C acid as a possible intermediate. The major hydrolysis products observed solely at pH 7.0 and pH 9.0 were formed by cleavage of the side chain amide linkage to produce Polyoxin d2 or rearrangement of the side chain to produce Polyoxin d1a and Polyoxin d1b. These products may also be degraded to uracil-5-carboxylic acid via Polyoxin C acid.

Water, Fish, and Irrigated Crops (OCSPP 860.1400)

The submitted waiver request (MRID 48653307) regarding water, fish and irrigated crop is **ACCEPTALE.** Polyoxin D Zinc Salt is not currently registered for uses that could result in residues in potable water, fish and irrigated crops. Environmental fate data were summarized for the degradation routes of hydrolysis, aqueous photolysis, and aerobic soil metabolism, and it was argued that if new aquatic uses were registered, no significant residues would be anticipated due to the rapid environmental degradation of polyoxin D Zinc Salt.

Photodegradation in Water (OCSPP 835.2240)

The photolysis study (MRID 48653305) is **ACCEPTABLE**. The photolytic degradation of [^{14}C]Polyoxin D was analyzed in an 11-day study in sterile buffers at pH 5.0, pH 7.0, pH 9.0, and sterile natural water. At intervals during incubation, aliquots were collected from each sample and analyzed directly by high-performance liquid chromatography with radiochemical flow detection (HPLC-RAD) to determine the distribution of radioactivity

and identification of degradation products. The net photolytic half-lives of [^{14}C]Polyoxin D were calculated to be 0.4 days, 4 days, 2.4 days, and 1.6 days in sterile natural water, pH 5.0, pH 7.0, and pH 9.0 buffers, respectively.

Photolytic degradation proceeded initially through cleavage of the pyrimidinyl linkage to produce the corresponding Uracil-5-Carboxylic Acid probably via Polyoxin C acid as a possible intermediate. Further degradation of Polyoxin D was formed by cleavage of the side chain amide linkage to produce Polyoxin d2 or rearrangement of the side chain to produce Polyoxin d1a and Polyoxin d1b. Unknown degradate having the estimated molecular weight of 475 (10.9-minute unknown) was also detected. Further photochemical degradation of Polyoxin D and/or its degradates led to formation of a complex mixture of polar components in the pH 5.0 buffer, pH 7.0 buffer, pH 9.0 buffer and natural water solutions. Based on the results of this study, photolysis will be a viable route of elimination of Polyoxin D from the environment.

Environmental Fate Summary

The submitted environmental fate data (MRID 48653303) is **ACCEPTABLE**. This submission is a summary of environmental fate data of polyoxin D zinc salt and contains duplicative information presented in the hydrolysis study (MRID 48653304), the photodegradation in water study (MRID 48653305), and the aerobic soil metabolism study (MRID 48653306). The summary information is presented to support the petition for exemption of requirement of a tolerance for residues polyoxin D zinc salt on all food and feed commodities.

Aerobic Soil Metabolism (OCSPP 835.4100)

The study of aerobic soil metabolism (MRID 48653306) is **ACCEPTABLE**. The aerobic soil metabolism of [^{14}C]Polyoxin D was determined with an agricultural soil from Saitama, Japan in soil test systems incubation at 25 ± 2°C in the dark for 90-days. At intervals during incubation, radiolabeled $^{14}CO_2$ was collected and extracts of soil were analyzed directly by high-performance liquid chromatography with radiochemical flow detection (HPLC-RAD) to determine the distribution of radioactivity and identification of degradation products. Polyoxin D was degraded rapidly under the aerobic soil conditions employed in this study with the major soil metabolites identified as Polyoxin C acid and $^{14}CO_2$. The Polyoxin C acid increased to maximum levels at Day 14 and then steadily declined in the aerobic soil. The amount of $^{14}CO_2$ steadily increased throughout the study as Polyoxin D declined in the system. The minor degradation products of Polyoxin D were Uracil-5-Carboxylic Acid and unknown metabolites at 3.3-, 3.6-, 11.3- and 30-minutes were observed at low levels and decreased to the end of the study.

The DT_{50} values for degradation of Polyoxin D in the aerobic soil test system were estimated using a linear regression analysis. The DT_{50} values were 15.9 and 59.2 days for the aerobic soil and sterile aerobic soil, respectively.

Under aerobic soil metabolism conditions using microbially active soils, Polyoxin D was metabolized rapidly. Based on the results of this study, Polyoxin D should dissipate under aerobic soil conditions from natural soil systems.

UV/Visible Absorption (OCSPP 830.7050)

The study of UV/Visible Absorption (MRID 48653302) is **ACCEPTABLE.** A laboratory study was conducted to determine the UV/visible absorption of Polyoxin D Zinc Salt by spectrophotometer analysis. The UV absorbance of Polyoxin D Zinc Salt in neutral, acidic and basic solutions was 270.0 nm, 274.0 nm and 268.5 nm, respectively.

Algal Toxicity (OCSPP 850.5400)

Methods and Materials (MRID 48660403)

Test Species: Green alga, *Selenastrum capricornutum*, strain ATCC22662.

Test Material: Polyoxin D zinc salt technical. The test solutions were prepared by dissolving Polyoxin D zinc salt in 2% 2Na·EDTA.

Test Concentrations: The final test concentrations were selected on the basis of results from a preliminary algal study which utilized Polyoxin D zinc salt concentrations of 3, 10, 30 and 100 mg/L. In the preliminary study the NOEC was around 3 mg/L and the EC_{50} was 3-10 mg/L.

Study Protocol: The test solutions were prepared in 100 ml water with an OECD-recommended culture medium (Table 2). The tests were conducted in 200 mL Erlenmeyer flasks under sterile, shaken (100 rpm) culture conditions (23.0-23.4°C, 4456-4638 Lux continuous illumination at 400-700 nm). The pH of the test solutions (8.0-8.2) was not adjusted. The initial cell density was 1.1×10^4 cells/mL. The exposures were for 72 hr. Cell densities in the cultures were determined at 24, 48 and 72 hr with a flow cytometer. There were three replicates for each test concentration and control.

Results

It was reported that there were no unexpected circumstances that may have had adverse effects on the reliability of the study. Observations made at the end of the study did not reveal any algal abnormalities in any of the test solutions.

Algal cell densities in each replicate at each time interval (0, 24, 48, and 72 hr). The mean algal cell counts at 72 hr were 46.1×10^4 cells/mL in the untreated control; 32.2×10^4 cells/mL in the solvent control; 43.6×10^4 cells/mL at 3 mg/L; 30.9×10^4 cells/mL at 4 mg/L; 38.6×10^4 cells/mL at 5 mg/L; 5.9×10^4 cells/mL at 7 mg/L; and 1.8×10^4 cells/mL at 10 mg/L.

Relative to solvent controls, growth inhibition was significantly ($p \leq 0.01$) different at nominal concentrations of 7 mg/L (78.8%) and 10 mg/L (95.2%). Algal growth inhibition rates, based on the growth rates (I_m) for 24-48 hr, are shown in Table 5; and algal growth inhibition rates, based on the growth rates (I_m) for 24-72 hr. Relative to solvent controls, growth inhibition for 24-48 hr, was significantly ($p \leq 0.01$) different at nominal concentrations of 7 mg/L (45.0%) and 10 mg/L (88.6%), and that for 24-72 hr significantly ($p \leq 0.01$) different at nominal concentrations of 7 mg/L (51.0%) and 10 mg/L (92.36%).

EC_{50} and NOEC values were calculated or estimated by comparing the algal cell growth inhibition in the treated solutions with that of the solvent control because "the stronger inhibition was observed in the solvent control group compared with the control group". Based on the areas under the curve, the E_bC_{50} (0-72 hr) was 6.47 mg/L (95% CI = 6.31-6.63 mg/L), and the $NOEC_b$ (0-72 hr) was 5 mg/L. Based on growth rate data, the E_rC_{50} (24-48 hr) was 7.19 mg/L (95% CI = 6.94-7.47 mg/L), and the NOEC was 5 mg/L; and the E_rC_{50} (24-72 hr) was 7.05 mg/L (95% CI = 6.84-7.28 mg/L), and the NOEC was 5 mg/L.

Conclusions:

The submitted study of Algal Toxicity (OCSPP 850.5400) is **ACCEPTABLE.** The test showed measured concentrations at the start and at the end of the test period. Growth inhibition was significantly different from the solvent control at concentration levels 6.09 mg/L and 8.80 mg/L. Based on the results, the E_bC_{50} (0-72 hr) was 6.47 mg/L (95% CI = 6.31-6.63 mg/L), and the $NOEC_b$ (0-72 hr) was 5 mg/L. Based on growth rate data, the E_rC_{50} (24-48 hr) was 7.19 mg/L (95% CI = 6.94-7.47 mg/L), and the NOEC was 5 mg/L; and the E_rC_{50} (24-72 hr) was 7.05 mg/L (95% CI = 6.84-7.28 mg/L), and the NOEC was 5 mg/L.

Non-target Insect Testing (OCSPP 880.4350)

The objective of the study was to test the oral toxicity of Polyoxin D zinc salt to the honeybee (*Apis mellifer*). For the Polyoxin D zinc salt treatments, 150, 75, 37.5, 18.75, or 9.375 µg was diluted with 20 µL of a 50% sucrose solution to make five dosage levels. Each dose of the test material (200 µL) was injected into a feeding tube with a micropipette, and the tube was inserted into one end of the test container into which 10 bees had been placed. Exposures were for approximately 3 hrs during which time the test containers were kept in an incubator. The actual dose levels were calculated from specific gravity measurements and the decrease in the feeding tube weights. Dimethoate was used as a reference material. Controls were untreated. There were five replicates per treatment and control. At the lowest oral dose tested (9.2616 µg/bee), Polyoxin D zinc salt was toxic to honeybees, with 8% mortality after 96 hr. The 96-hr LD_{50} was 28.77µg/bee.

Conclusion:

The submitted study for insect testing is **ACCEPTABLE.** Polyoxin D zinc salt was toxic to honeybees, with 8% mortality after 96 hr. The 96-hr LD_{50} was 28.77µg/bee.

Prenatal Developmental Toxicity Study - Rat; OCSPP 870-3700

(MRID 4853315) In a teratology (developmental toxicity) study (MRID 48653315), Polyoxin D zinc salt (204, Lot/batch No. 124-164-W9-00) in 5% methylcellulose was administered by gavage to groups of 24 mated and presumed pregnant female Br/Han:WIST@Jcl (GALAS) rats at doses of 0, 100, 300, or 1000 mg/kg bw/day from gestation day (GD) 6-19 inclusive. One dam in the control group not pregnant was not evaluated. The dams were killed on GD 20 for examination of uterine content. The fetuses were examined externally, sexed, and weighed. Approximately one-half the fetuses were examined for visceral variations and anomalies and the remaining half was fixed, stained, and cleared for examination of skeletal variations and anomalies.

No deaths or changes in general appearance were observed in maternal rats treated with any dose of Polyoxin D zinc salt. Body weight, weight gain, body weight adjusted for gravid uterine weight, and food consumption were not adversely affected by treatment with the test substance. At necropsy, 20/24 maternal rats administered 1000 mg/kg/day had thickening of the limiting ridge in the stomach compared with 0/23 controls. This lesion was not observed at 100 or 300 mg/kg/day.

Therefore, the lowest-observed-adverse-effect level (LOAEL) for maternal toxicity of Polyoxin D zinc salt in rats is 1000 mg/kg bw/day based on gross lesions in the stomach (thickening of the limiting ridge). The no-observed-adverse-effect level (NOAEL) is 300 mg/kg bw/day.

No treatment-related effects were observed on developmental parameters including gravid uterine weight, placental weight, mean numbers of corpora lutea and implantation sites, numbers of early and late resorptions (dead or resorbed embryos or fetuses), number of live fetuses per dam, implantation index, viability index, sex ratio, and male and female fetal body weight. The incidence of external, visceral, and skeletal variations and anomalies were not affected by treatment with Polyoxin D zinc salt.

Conclusions:

The developmental toxicity study in the rat is classified **ACCEPTABLE** and satisfies the guideline requirement for a developmental toxicity study (OCSPP 870.3700; OECD 414) in the rat. The developmental toxicity LOAEL for Polyoxin D zinc salt is not determined. The NOAEL is ≥1000 mg/kg bw/day.

Mutation Assay OCSPP 870.5100

In a reverse gene mutation assay in bacteria (MRID 48653313), *S. typhimurium* strains TA98, TA100, TA1535, and TA1537 and *E. coli* strain WP2 *uvrA* were exposed to

Polyoxin D zinc salt (technical grade, chemical purity not given, lot number PSB-625) dissolved in DMSO, without and with activation, in a pre-experiment for cytotoxicity and in two independent mutation assays each using the pre-incubation method. The pre-test cytotoxicity assay used single plates at concentrations of 0, 1.2, 4.9, 19.5, 78.1, 313, 1250, and 5000 µg/plate. The first mutation assay used concentrations of 0, 61.7, 185, 556, 1667, and 5000 µg/plate and the second mutation assay used 0, 313, 625, 1250, 2500, and 5000 µg/plate. All mutation assays were done using triplicate plating. The S9 fraction was obtained from phenobarbital + 5,6-benzoflavone-induced male Sprague Dawley rat liver.

The test material Polyoxin D zinc salt was tested at concentrations up to the limit concentration for the assay, and there was no evidence that the assays were affected by cytotoxicity or insolubility. The number of revertants per plate was not significantly increased, never reaching 2x the concurrent solvent control value, at any test article concentration, with or without S9-mix, in any tester strain. The solvent and positive controls induced the appropriate responses in the corresponding strains and were in agreement with the historical control data from this laboratory. There was no evidence of induced mutant colonies over background.

Conclusions:

The submitted gene mutation assay is **ACCEPTABLE.** There was no evidence of cytotoxicity or insolubility. Acceptable experimental protocols were followed, and solvent and positive control values were appropriate for the respective strains. The test article did not increase the mean number of revertants per plate by a factor of two or more over the corresponding solvent control values for any of the five strains tested at any of the tested concentrations, without or with S9-mix. None of the experimental numbers of revertant colonies even approached a number that would suggest a biologically significant positive result, even at the limiting dose of 5000 µg/plate.

In Vitro Mammalian Chromosome Aberration Test OCSPP 870.5375

In a mammalian cell cytogenetics assay for chromosome aberrations (MRID 48653314), cultured Chinese hamster lung cells (CHL/IU) were exposed to Polyoxin D Zinc Salt (technical grade, chemical purity not given, Batch PSB-625) dissolved in dimethylsulfoxide. In Exp. I, cells were exposed without activation for 6 hours, at concentrations of 0, 67.7, 94.8, 133, 186, and 260 µg/mL and were exposed with activation for 6 hours at concentrations of 0, 19.8, 59.3, 178, 533, and 1600 µg/mL. After treatment, the test article was removed from the cultures and replaced with fresh medium and the cells were allowed to recover for 18 hours before fixation. In Exp. II, cells were exposed without activation continuously for 24 hours at concentrations of 0, 34.5, 48.3, 67.7, 94.8, and 133 µg/mL followed by fixation and analysis. The S9 used for activation was obtained using livers of Sprague-Dawley male rats induced with phenobarbital and 5,6-benzoflavone and obtained commercially.

In Experiment I Polyoxin D Zinc Salt was tested up to dose levels that caused >50% cell lethality without activation (260 µg/mL) and with activation (1600 µg/mL). Without activation, the frequencies of the metaphases with structural chromosome aberrations (excluding gaps) were 14.5% and 7.5% at test article concentrations of 186 and 260µg/mL, respectively. These were statistically highly significant ($p \leq 0.001$) increases over the solvent control; with activation, the frequency of metaphase cells with structural chromosome aberrations (excluding gaps) was 9.5% at a test article concentration of 1600 µg/mL, which was a statistically highly significant ($p \leq 0.001$) increase over the solvent control. There was also precipitation of the test article at this concentration. The frequency of polyploid metaphase cells showed no increases either without or with activation. In Experiment II, a 24 hour continuous treatment without activation resulted in a 8.0% frequency of metaphases with structural chromosome aberrations (excluding gaps) at the concentration of 133 µg/mL, which was a statistically highly significant ($p \leq 0.001$) increase over the solvent control. There were no increases in the frequency of polyploid metaphases. All of the solvent and positive controls gave appropriate responses in both experiments and were within the ranges of the corresponding historical controls.

Conclusions: The submitted cell cytogenetics assay is classified as **ACCEPTABLE** and satisfies the guideline requirement for Test Guideline OCSPP 870.5375 [*In vitro* mammalian chromosome aberration test; OECD 473] for *in vitro* cytogenetic mutagenicity data.

Reasonable Grounds in Support of the Petition (OCSPP 860.1560)

The registrant summarized data submitted in separate data volumes to support petition for expanding exemption from the requirement of a tolerance the residues of the biochemical pesticide polyoxin D zinc salt in all agriculture commodities. The petitioner has provided the following acceptable arguments:

1. Both the chemical identity and product chemistry of Polyoxin D Zinc Salt are known.
2. The registered directions for the use of this chemical in the United States and in the rest of the world are known. Current and future uses of this chemical are limited by the high cost of treatment using this chemical relative to other fungicides and by the need to alternate the use of fungicides with different modes of action to minimize the potential for the development of resistance. These practical limitations make it unlikely that approval of a tolerance exemption for all food and feed commodities will cause problems from increases in the number of uses and in application rates.
3. Polyoxin D Zinc Salt is an anti-fungal fermentation product that is produced by a bacterium that occurs naturally in the soil.
4. This chemical has a non-toxic mode of action that is specific to fungi because it inhibits synthesis of cell wall chitin in fungi. Instead of killing fungi, it simply stops fungal growth. Humans and other mammals have cell membranes, but they no not have cell walls or structures that contain chitin. Polyoxin D Zinc Salt in not

effective as an anti-bacterial agent, and it has never been used in human or veterinary medicine.

5. The toxicology of this chemical is well understood, with more data available than are usually available for biochemicals. These data show that Polyoxin D Zinc Salt has low acute, subacute, chronic, and developmental toxicity, that it is not mutagenic *in vivo*, that it has low immunotoxicity and reproductive toxicity, and that it is not oncogenic.
6. Data suggest that this chemical is not an endocrine disruptor.
7. The nature of the residue in plants is understood and has been shown to be the same in three dissimilar crops, namely grapes, tomatoes and head lettuce. The primary residues are Polyoxin D and Uracil-5-carboxylic acid. These two residues are further metabolized to a large number of small molecule metabolites, each of which is present at levels too low to require identification.
8. The studies of the nature of the residue in plants are supported by storage-stability data, by acceptable recoveries from spiked samples, and by acceptable mass balance (that is, accounting for the total radioactive residues).
9. Based on the available crop metabolism data and environmental fate data, there is thought to be an adequate understanding of the nature of the residue in ruminants and poultry. As in plants, the anticipated residues are expected to be Polyoxin D and Uracil-5-carboxylic acid. Rapid elimination of residues is expected in the urine.
10. Also based on the available crop metabolism data and environmental fate data, residues resulting from treatments with this chemical according to good agricultural practices are expected to be low in raw agricultural crop commodities, processed agricultural crop commodities, meat, milk, poultry, eggs, potable water, fish (should there be any possible future uses on aquatic crops), and drinking water.
11. Based on the crop metabolism data, significant reduction of Polyoxin D residues is easily achieved by simply rinsing raw agricultural commodities with water. Based on the hydrolysis data, a further reduction in residues would be expected to result from cooking.
12. Because Polyoxin D Zinc Salt has low toxicity and very low dietary exposure levels, the dietary risk from this chemical should be very low.

Risk Characterization

An exemption from the requirement of a tolerance has been established for the residues of the biochemical pesticide polyoxin D zinc in 40 CFR 180.1285 when used as a fungicide on almonds, cucurbit vegetables, fruiting vegetables, ginseng, grapes, pistachios, pome fruits, potatoes and strawberries.

The submitted toxicological studies of acute (six-pack) toxicity, mutagenicity, subchronic (90-day oral), developmental, and chronic/oncogenicity support the existing tolerance exemption in 40 CFR 180.1285 for the biochemical pesticide polyoxin D zinc. Although the studies indicate a lack of toxicity hazards for mammals; however, EPA concluded that

there is a reasonable certainty of no harm to humans, including infants and children; from the proposed food uses of polyoxin D zinc salt.

Developmental Toxicity

A new developmental study (MRID 48653315) was contacted for polyoxin D zinc salt to support the expansion of the tolerance exemption. No treatment-related effects were observed in general appearance, body weight, body weight adjusted for gravid uterine weight, weight gain, or food consumption in maternal rats at the doses tested (0, 100, 300, and 1000 mg/kg bw/day). Necropsy observations showed that almost all rats (20/24) in the 1,000 mg/kg/day group (highest dose tested) had thickening of the limiting ridge. Therefore, the lowest observed adverse effect level (LOAEL) for maternal toxicity of polyoxin D zinc salt in rats is 1,000 mg/kg bw/day based on gross lesions in the stomach (thickening of the limiting ridge). The no observed adverse effect level (NOAEL) for maternal toxicity is 300 mg/kg bw/day based on no effects observed at this dose. Although an effect of gross lesions in the stomach was found in maternal rats at the limit dose tested (1,000 mg/kg bw/day), there were no reported systemic effects in maternal rats at this dose. The effect in the stomach lining was limited to a localized gastric irritation due to the route of entry (oral gavage) at the limit dose tested (1,000 mg/kg bw/day), which is typical of the nature of the test substance.

The developmental toxicity showed that no treatment-related effects were observed on developmental parameters including gravid uterine weight, placental weight, mean numbers of corpora lutea and implantation sites, numbers of early and later resorptions (dead or resorbed embryos or fetuses), number of live fetuses per dam, implantation index, viability index, sex ratio, and male and female body weight. The incidence of external, visceral, and skeletal variations and anomalies were not affected by treatment of polyoxin D zinc salt. Based on no effects observed for developmental toxicity at any doses tested, the NOAEL for developmental toxicity is greater than 1,000 mg/kg bw/day (highest dose tested). The LOAEL was not identified for developmental toxicity, suggesting that the test animals could have tolerated a higher dose.

The submitted developmental toxicity data and the previous submitted toxicity studies of Tier III two-generation reproduction indicate that no reproductive effects at the limit dose tested. The toxicity profile is adequately determined that polyoxin D zinc salt is not a developmental toxicant. The consumption of food commodities that are treated with polyoxin D zinc salt when used as a pesticide will not be harmful to human health from dietary exposure.

Mutagenicity Studies

Two new mutagenicity studies were conducted for polyoxin D zinc salt to support the expansion of the tolerance exemption. The mutagenicity studies along with the mutagenicity studies submitted to support the previous tolerance exemption. The studies determined that polyoxin D zinc salt is not a mutagen. The consumption of food

commodities that are treated with polyoxin D zinc salt when used as a pesticide will not be harmful to human health from dietary exposure.

1. A reverse gene mutation assay in bacteria (MRID 48653313) using the technical grade of polyoxin D zinc salt, dissolved in dimethyl sulfoxide (DMSO), with and without metabolic S9 activation, showed no mutagenic effects or evidence of cytotoxicity or insolubility even at the limiting dose of 5000 ug/plate (Ref. 1). Therefore, polyoxin D zinc salt is considered to be non-mutagenic under the conditions of this assay.

2. An *in vitro* mammalian chromosome aberration test (MRID 48653314) using the technical grade of polyoxin D zinc salt, dissolved in DMSO, with and without metabolic S9 activation, showed clastogenic potential in Chinese hamster lung cells (CHL/IU) with and without activation. In Experiment I, polyoxin D zinc salt was tested up to dose levels that caused >50% cell lethality without activation (260 µg/mL) and with activation (1600 µg/mL). Without activation, the frequencies of the metaphases with structural chromosome aberrations (excluding gaps) were 14.5% and 7.5% at test article concentrations of 186 and 260µg/mL, respectively. With activation, the frequency of metaphase cells with structural chromosome aberrations (excluding gaps) was 9.5% at a test article concentration of 1600 µg/mL. The frequency of polyploid metaphase cells showed no increases either without or with activation. In Experiment II, a 24-hour continuous treatment without activation resulted in a 8.0% frequency of metaphases with structural chromosome aberrations (excluding gaps) at the concentration of 133 µg/mL. There were no increases in the frequency of polyploid metaphases.

Although the submitted *in vitro* mammalian chromosome aberration test showed clastogenic potential, the results were not reproducible at the dose levels reported in the experiment. In addition, the mutagenicity data submitted to support the previous tolerance exemption, which included three complimentary Tier I mutagenicity tests and a Tier II mammalian erythrocyte micronucleus *in vivo* test, showed no mutagenic effects including no clastogenic potential (no chromosomal aberrations). Furthermore, the lack of systemic toxicity noted in the following developmental toxicity section indicted no effects in the Tier III two-generation reproduction study. The studies indicate that polyoxin D zinc salt is not mutagenic or clastogenic. The studies support this expansion of the tolerance exemption based on the weight of evidence of the mutagenicity data.

Proposed Tolerances (OCSPP 860.1550)

Kaken Pharmaceutical Co., Ltd. proposes that §180.1285 are amended as follows (MRID48653307): **"§180.1285 Polyoxin D zinc salt; exemption from the requirement of a tolerance.** An exemption from the requirement of a tolerance is established for the residues of the biochemical pesticide polyoxin D zinc salt in or on all agricultural commodities when polyoxin D zinc salt is used as a fungicide in accordance with good agricultural practices." The study makes this request and provides no further argument in this section. It does, however, point out a typographical error in the spelling of the CAS chemical name of Polyoxin D Zinc Salt that occurred on page 69559 of the November 19, 2008, Federal Register. The letters "in" at the end of the published chemical name are

extraneous letters. The correct CAS chemical name for polyoxin D zinc salt, based on the ninth chemical index and a search of the CAS database and expressed as salt, is: zinc 5-[[2-amino-5-*O*-(aminocarbonyl)-2-deoxy-L-xylonyl]amino]-1-(5-carboxy-3,4-dihydro-2,4-dioxo-1(2*H*)-pyrimidinyl)-1,5-dideoxy-β-D-allofuranuronate.

cc: C.Walsh; BPPD Chron File; OHAD/ARS
M. Xue, BPPD, 05/11/12