US Environmental Protection Agency
Office of Pesticide Programs

BIOPESTICIDE REGISTRATION ACTION DOCUMENT
STREPTOMYCES LYDICUS WYEC 108

(PC Code 006327)

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U.S. Environmental Protection Agency
Office of Pesticide Programs
Biopesticides and Pollution Prevention Division
Streptomyces lydicus WYEC 198
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Streptomyces lydicus WYEC 108
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I. EXECUTIVE SUMMARY/FACT SHEET

Active Ingredient and Proposed Use

The active ingredient, *Streptomyces lydicus*, is a ubiquitous and naturally-occurring bacterium that is commonly found in soil environments. The isolate WYEC 108 (PC Code 006327) was originally obtained from English agricultural soil and has been deposited in the American Type Culture Collection as culture number ATCC 55445. The end-use product, Actinovate Soluble (containing 1.0 % *Streptomyces lydicus* WYEC 108), is to be used as an antifungal agent for greenhouse, nursery, turf grass, and agricultural use sites. Applications of *Streptomyces lydicus* WYEC 108 as a soil mix are expected to control *Fusarium*, *Rhizoctonia*, *Pythium*, *Phytophthora*, *Phytomatotricum*, *Aphanomyces*, *Monosprascus*, *Armillaria*, *Sclerotinia*, *Postia*, *Verticillium*, *Geotrichum*, and other root decay fungi.

S. lydicus has been researched extensively in both the laboratory and under field conditions and has been described in scientific literature for over 45 years. As a "free living" saprophytic soil organism, *S. lydicus* has not been shown to have a specific fungal host range, yet the organism is readily isolated from soils and plant rhizospheres. The mode of action is as follows: *S. lydicus* colonizes growing root tips of plants and acts as a mycoparasite of fungal root pathogens which helps protect the plants. Other possible mechanisms include the production and excretion of antifungal metabolites (e.g., antibiotics and/or low molecular weight antifungal compounds or lytic enzymes like chitinase) after colonization.

Toxicology, Human Exposure and Risks

Evaluations of mammalian toxicology data comply with the Food Quality Protection Act (FQPA) of 1996, and are sufficient to support the unconditional registration of this microbial pesticide for the proposed uses. *Streptomyces lydicus* WYEC 108 is categorized as Toxicity Category IV for acute oral toxicity. Based on the acute oral toxicity study, the requirement for a separate toxicity/pathogenicity study for the TGAI was waived. Acute pulmonary and injection toxicity/pathogenicity studies demonstrated no toxicity or infectivity potential for *S. lydicus* WYEC 108. A data waiver was accepted for acute dermal toxicity/pathogenicity based on the lack of toxicity and infectivity demonstrated by the submitted oral, pulmonary, injection, and irritation studies.

The submitted primary eye and dermal irritation studies showed that *S. lydicus* WYEC 108 is essentially non-irritating and is categorized as Toxicity Category IV for both exposures. The Agency has accepted requests to waive data for acute inhalation toxicity, hypersensitivity study, and immune response. The rationales for the data waiver requests were based on: a) the low toxicity and irritation potential as demonstrated by acute oral, pulmonary, injection toxicity/pathogenicity studies and eye and dermal irritation studies; b) clearance of the active

ingredient in the injection study; and e) no documented reports of hypersensitivity incidents during production and testing of the active ingredient and end use product [Table 2b and discussion in Section III.B.2].

Food Tolerances

For this section 3(c)(5) unconditional registration, a permanent tolerance exemption is being established in 40 CFR 180.1253 for residues of *Streptomyces lydicus* WYEC 108 on all agricultural commodities when used/applied in accordance with label directions.

FQPA Considerations

The Agency has considered *Streptomyces lydicus* WYEC 108 in light of the safety factors of the Food Quality Protection Act (FQPA) of 1996 and has made a determination of reasonable certainty of no harm to the U.S. population in general, and to infants and children in particular. The ubiquitous occurrence of *S. lydicus* suggest that humans are commonly exposed to the microbe regardless of treatment with *S. lydicus* WYEC 108. Thus, applications of *S. lydicus* WYEC 108 are not expected to increase exposure above normal background levels [Section III.B.3].

No toxicity endpoints were indicated to justify setting a numerical tolerance for *S. lydicus* WYEC 108. Based on submitted studies, *S. lydicus* WYEC 108 demonstrates low acute oral toxicity potential (Toxicity Category IV), indicating no incremental dietary risk [Section III.B.3].

In this assessment, no acute, subchronic, chronic, immune, endocrine, or non-dietary exposure issues have been identified which may have any incremental adverse effects on infants, children, and the general U.S. population. Based on the Toxicity Category IV for acute oral and pulmonary toxicity effects, a safety factor is not required for residues of *S. lydicus* WYEC 108. The potential transfer of *S. lydicus* WYEC 108 residues to human adults, infants, and children via dietary exposure is not likely to be greater than exposure to current existing levels of naturally-occurring *S. lydicus*. Potential risks via exposure to drinking water or runoff are not expected because *S. lydicus* WYEC 108 does not thrive in aquatic environments [Section III.B.5].

The potential for aggregate, non-occupational exposure is unlikely because the use sites for *S. lydicus* WYEC 108 are agricultural and horticultural. However, since *S. lydicus* is a common, naturally-occurring soil bacterium, there is a great likelihood of prior exposure for most, if not all individuals. Accordingly, the increase in exposure due to the use of *S. lydicus* WYEC 108 would be negligible. There have been no documented reports of hypersensitivity during the research and manufacture of *S. lydicus* WYEC 108. Furthermore, no mechanism of pathogenicity or toxicity in mammals has been identified for *S. lydicus* WYEC 108 and the organism is considered non-toxic to mammals. Thus, exposure to *S. lydicus* WYEC 108 is not

likely to pose any incremental risk to humans, infants, and children.

Occupational and Residential Exposure and Risk

Potential exposure to workers and pesticide handlers from *Streptomyces lydicus* WYEC 108 is not expected to pose any undue risk. Pesticide drift is minimized because the end use product is only applied outdoors as a soil drench and is not applied aerially. Foliar applications are for greenhouse use only. Appropriate Personal Protective Equipment (PPE) and a Restricted Entry Interval (REI) of 4 hours for foliar greenhouse applications are required to mitigate any potential risks to workers and pesticide handlers. Residential exposure and risk are not expected because *S. lydicus* WYEC 108 is applied to agricultural and horticultural sites and is non-toxic/non-pathogenic to mammals.

Ecological and Environmental Exposure and Risks

Non-target toxicity tests were waived for all indicator species, except freshwater fish. The freshwater fish test revealed no toxicity to rainbow trout at the concentrations tested. Waivers for the remaining non-target studies were granted due to 1) the results observed in the freshwater fish study, 2) lack of exposure for most non-target species, 3) *Streptomyces lydicus* WYEC 108 is a ubiquitous, naturally-occurring soil bacterium, and 4) scientific literature citations demonstrating lack of toxicity to non-target organisms among similar *Streptomyces* spp. No incremental risks to non-target organisms are expected from use of *S. lydicus* WYEC 108 as labeled.

Data Gaps and Requirements/Labeling

There are no data deficiencies for *Streptomyces lydicus* WYEC 108. However, if more extensive use patterns are sought for treatment of other agricultural terrestrial sites or crops, additional information and data may be required on a case-by-case basis.

II. OVERVIEW

A. Product Overview

Biological Name: *Streptomyces lydicus* WYEC 108

ATCC Number: 55445

Trade and Other Names: Actinovate

OPP Chemical Code: 006327

Basic Manufacturer: Natural Industries, Inc.
6223 Theall Road
Houston, Texas 77066

B. Use Profile

The following is information on the proposed uses with an overview of use sites and application methods.

Type of Pesticide: Fungicide

Use Sites: Greenhouse crops, nursery crops, ornamentals, turf grass

Target Pests: Root rot and damping-off fungi including *Fusarium*, *Rhizoctonia*, *Phytophthora*, *Pythium*, *Phytomatotricum*, *Aphanomyces*, *Monosprascus*, *Armillaria*, *Sclerotinia*, *Postia*, *Verticillium*, and *Geotrichum*. Foliar fungal pathogens including *Botrytis* and powdery mildew.

Formulation Types: Solid, water soluble powder.

Method and Rates of Application: Applied as a soil mix/drench to potted plants or turf grass or to plant foliage in greenhouses. Application rates for soil mix are 6 oz. end product per 100 gallons water (1 gallon solution into 1 cubic foot of soil mix). For turf grass, rate is 52 oz. dissolved end product per acre (initial application) and 18 oz. per acre (maintenance treatments). Foliar application (greenhouse) is 6-12 oz. end product dissolved in water per acre.

Use Practice Limitations: Not for use with irrigation systems.

Timing: For soil mix/drench, one initial application. For turf grass, one initial application, plus maintenance applications every 6-8 weeks. For greenhouse foliar applications, every 7-14 days depending on pest pressure.

C. Estimated Usage

An estimate of usage based on existing commercial use cannot be made since this is the first registration containing *Streptomyces lydicus* WYEC 108 as the active ingredient. There have been no Experimental Use Permits (EUPs) issued for products containing *S. lydicus* WYEC 108.

D. Data Requirements

The data and information submitted in support of this unconditional registration under section 3(c)(5) of the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) have been reviewed by the Biopesticides and Pollution Prevention Division (BPPD). For *Streptomyces lydicus* WYEC 108, the product identity and analysis data, as well as the information submitted for acute mammalian toxicity and ecological effects are sufficient to allow the proposed use patterns. Based on evaluations of the submitted data and information, as discussed in this document, the Agency foresees no unreasonable adverse effects to human health and the environment from the use of *S. lydicus* WYEC 108, as long as it is used as labeled.

E. Regulatory History

Experimental Use and Temporary Tolerance Exemption

No Experimental Use Permits (EUPs) or temporary tolerance exemptions have been issued for *Streptomyces lydicus* WYEC 108.

Section 3 Registration and Exemption from tolerance

EPA received an application from Natural Industries, Inc., 6223 Theall Road, Houston, TX 77066 on April 27, 2000 to register the active ingredient *Streptomyces lydicus* WYEC 108. When the application package was deemed complete, the receipt of the application for the new active ingredient was published in the Federal Register [FR: October 4, 2000, Vol. 65, No. 193, page 59185]. No comments to the FR announcement were received by the Agency.

Concomitant with the application for the Section 3(c) registration, the registrant filed a petition (PP 0F6163) requesting a permanent exemption from the requirement of a tolerance for

the active ingredient, *S. lydicus* WYEC 108, on all agricultural commodities. A notice of filing of this petition was published in the Federal Register [FR: August 1, 2000, Vol. 65, No. 148, page 46912]. No comments to the FR announcement were received by the Agency. An exemption from the requirement of a tolerance for residues of *S. lydicus* WYEC 108 on all agricultural commodities is being processed in connection with this petition and the final rule will be published in the Federal Register (40 CFR 180.1253), concurrent with the conditional registration.

III. SCIENCE ASSESSMENT

A. Physical and Chemical Properties Assessment

The data submitted in support of product identity requirements for *Streptomyces lydicus* WYEC 108 are sufficient for the proposed use patterns of the microbial pesticide.

1. Product Identity and Mode of Action

Streptomyces lydicus WYEC 108 is a ubiquitous and naturally-occurring soil microorganism. *S. lydicus* has been researched extensively in the laboratory and field and has been described in the scientific literature for approximately 45 years. As a "free-living" and saprophytic soil organism, *S. lydicus* has not been shown to have a specific fungal host range, yet the organism is readily isolated from soils and plant rhizospheres. The mode of action is as follows: *S. lydicus* colonizes the growing root tips of plants and acts as a mycoparasite of fungal root pathogens to protect plants. Other possible mechanisms include the production and excretion of antifungal metabolites after colonization (e.g., antibiotics and/or low molecular weight antifungal compounds or lytic enzymes such as chitinase).

The isolate WYEC 108 was originally obtained from English agricultural soil. It is similar to another saprophytic *Streptomyces*, *S. griseoviridis*, which was first isolated from peat moss in Finland and is currently used as a pesticide in agricultural and forestry applications. *Streptomyces lydicus* WYEC 108 is on deposit at the American Type Culture Collection (Rockville, MD) as culture number ATCC 55445. [MRID 451413-01; BPPD Review, October 15, 2001]

2. Physical and Chemical Properties Assessment

Streptomyces lydicus WYEC 108 can be described as spiral-chained, reddish, smooth-surfaced conidia spores. The vegetative mycelium is filamentous without spores. The isolate also has the following characteristics: it does not produce melanin or H_2S pigment when growing on peptone-yeast-iron agar or peptone-iron agar, it grows between pH 5.6 and 8.0 with an optimal temperature of ≈ 30° C (but will grow at 37° C), and white colonies initially form aerial mycelia which become gray. *Streptomyces lydicus* WYEC 108 is similar in biochemical characteristics to ATCC 25740 (*Streptomyces lydicus*), with a slight difference in sporulation (- or +) with glucose, sucrose, galactose, inositol, xylitol, arabinose, and Na pyruvate. The isolate can be further identified utilizing viable plate counts on a selective medium containing antibiotics. *Streptomyces lydicus* WYEC 108 is resistant to carbenicillin (200 µg/ml), spectinomycin (10 µg/ml), streptomycin (10 µg/ml), neomycin (10 µg/ml), and ampicillin (100 µg/ml). The isolate is sensitive to chlorotetracycline (25 µg/ml), hygromycin (25 µg/ml), bacitracin (25 µg/ml), kanamycin (100 µg/ml), and erythromycin (100 µg/ml).

The end product is a solid (powder) with a pH of 6.6 (Table 1b). Guideline data requirements (40 CFR §158.740(a)) for melting point, boiling point, solubility, vapor pressure, dissociation constant, octanol/water partition coefficient, stability, oxidizing or reducing potential, flammability/flash point, explodability, viscosity, miscibility, and dielectric breakdown voltage were waived because of the nature of the microbial pesticide.

Table 1a: Product Identity & Manufacturing Process for *Streptomyces lydicus* WYEC 108

Guideline	Study	Result	MRID #
151-10 *885.1100	Product Identity	*S. lydicus* WYEC is a ubiquitous, naturally-occurring soil microorganism that colonizes root tips and acts as a mycoparasite. ACCEPTABLE	451413-01
151-11 *885.1200	Manufacturing Process	ACCEPTABLE	451413-01 460572-01
151-12 *885.1300	Discussion of Formation of Unintentional Ingredients	No toxicological impurities are associated with the active ingredient. If microbial contamination occurs, lots are autoclaved and discarded. ACCEPTABLE	451413-01
151-13 *885.1400	Analysis of Samples	Samples were analyzed prior to mixing with final inert ingredients. Quantification of spores was done by plate counts from five batches. ACCEPTABLE	451413-01 460572-01
151-15 *885.1500	Certification of limits	Certified limits are within OPPTS guidelines. ACCEPTABLE	451413-01 460572-01 CSF
151-16	Analytical Method	Spore concentration is determined by basic spread plate methods. Serial dilutions of spore preparations are plated and incubated. CFU counts and contamination are recorded. ACCEPTABLE	451413-01

*OPPTS Harmonized Guidelines

Table 1b: Physical & Chemical Properties of *Streptomyces lydicus* WYEC 108

	Physical/Chemical Properties		
Guideline	**Study**	**Result**	**MRID #**
151-17	physical state	Solid (powder)	451413-01
	pH	pH 6.6 for end product; active ingredient grows between pH 5.6 - 8.0	451413-01 460572-01
	bulk density	Not applicable	451413-01
	storage stability	Stable for up to one year when stored in original packaging	451413-01

B. Human Health Assessment

1. Food Clearances/Tolerances

This is the first proposed Section 3(c)(5) unconditional registration of the subject strain, *Streptomyces lydicus* WYEC 108. There is a reasonable certainty that no harm is likely to result from exposure to *S. lydicus* WYEC 108. This includes all anticipated dietary exposures for which there is reliable information. As such, an exemption from the requirement of a food tolerance for residues of *S. lydicus* WYEC 108 is being established concomitant with the unconditional registration (40 CFR 180.1253). Below is the toxicology assessment, and discussion of other factors under the Food Quality Protection Act (1996), which led to the decision to grant the exemption from tolerance.

2. Toxicology Assessment

Mammalian toxicology studies have been submitted and are sufficient to support the unconditional registration of *Streptomyces lydicus* WYEC 108 for the proposed use patterns. Summaries of the acute toxicological studies (Table 2a) and the rationales for certain data waiver requests (Table 2b) are discussed below.

a. Acute Oral Toxicity (MRID 451117-01; OPPTS 870.1100)

Five male and 5 female Sprague-Dawley rats were dosed with formulated (end use product) *Streptomyces lydicus* WYEC 108 via oral gavage (MRID# 451117-01; BPPD Data Evaluation Report, dated October 15, 2001). During the observation period, no rats died, one female had diarrhea within 2 hours but recovered within 4 hours, one male had soft feces 4 hours after dosing with recovery by day 1, and three males exhibited piloerection on day 1 with recovery by day 2. All rats gained weight during the study and no rats had observable

abnormalities during gross necropsy examinations. The study was originally rated "supplemental" due to questions about the test material (BPPD review - October 15, 2001). The registrant addressed the questions in a letter dated February 28, 2002 and the study was subsequently upgraded to "acceptable" (BPPD Review dated May 21, 2003). With a LD_{50} > 5,050 mg/kg body weight, the pesticide was classified as Toxicity Category IV for acute oral toxicity.

Table 2a: Tier I - Acute Mammalian Toxicity of *Streptomyces lydicus* WYEC 108

Guideline	Study	Toxicity Category	Results	MRID #
152-30 *870.1100	Acute oral toxicity	IV	Acceptable. 5 male, 5 female Sprague-Dawley rats dosed - no rats died during the study. LD_{50} > 5,050 mg/kg	451117-01
152-32 *885.3150	Acute pulmonary toxicity/ pathogenicity	N/A	Acceptable. *S. lydicus* WYEC 108 was not toxic, infective, or pathogenic to rats. Clearance from liver and lymph nodes by day 7, kidneys by day 14, and lungs by day 28.	451117-02
152-33 *885.3200	Acute injection toxicity/ pathogenicity	N/A	Acceptable. *S. lydicus* WYEC 108 was not toxic, infective, or pathogenic to rats. Clearance from blood, kidney, and lymph nodes by day 14, lungs by day 21, and liver and spleen by day 28.	451117-03
152-34 *870.2500	Primary dermal irritation	IV	Acceptable. 3 rabbits dosed - 1 rabbit had very slight erythema with clearance by 24 hours.	451117-05
152-35 *870.2400	Primary eye irritation	IV	Acceptable. 3 rabbits dosed - conjunctival irritation was reduced by 24 hours and all irritation was resolved by 72 hours.	451117-04

* OPPTS Guideline Numbers**.**

b. Acute Pulmonary Toxicity/Pathogenicity (MRID 451117-02; OPPTS 885.3150)

Forty-eight male and 48 female Sprague-Dawley rats were given either a single intratracheal dose of 0.1 ml (9.1 x 10^8 cfu) of *Streptomyces lydicus* WYEC 108, an inactivated dose of *S. lydicus* WYEC 108, or were untreated (MRID# 451117-02; BPPD Data Evaluation Report, dated October 15, 2001). No rats died during the observation period and no abnormalities were observed in any rat during the gross necropsy examinations. Six rats from the treated and control groups lost weight before sacrifice on day 3 – all other rats gained weight during the study. Clinical signs were transient - all rats treated with inactivated *S. lydicus* WYEC 108 had piloerection on day 1 with recovery by day 2 and one female treated with active *S. lydicus* WYEC 108 walked on tiptoe with piloerection, raspy breathing and dark crust around the eyes which cleared by day 2. *S. lydicus* WYEC 108 was detected in lung, kidney, liver, and lymph nodes of the treated rats. Clearance from the liver and lymph nodes was established by day 7, from the kidneys by day 14, and from the lungs by day 28. Given the test results, *S. lydicus* WYEC 108 was not shown to be toxic, infective, or pathogenic to rats.

c. Acute Injection Toxicity/Pathogenicity (MRID 451117-03; OPPTS Guideline 885.3200)

Forty-two male and 42 female Sprague-Dawley rats were given either a single intravenous dose of 0.1 ml (9.33 x 10^8 cfu) of *Streptomyces lydicus* WYEC 108, an inactivated dose of *S. lydicus* WYEC 108, or were untreated (MRID# 451117-03; BPPD Data Evaluation Report, dated October 15, 2001). No rats died during the observation period. One female treated with inactivated *S. lydicus* WYEC 108 and 2 males and 3 females treated with active *S. lydicus* WYEC 108 lost or did not gain weight before sacrifice. All other rats gained weight during the study. No clinical abnormalities were observed in any of the treated rats during the study or the gross necropsy. *S. lydicus* WYEC 108 was detected in the blood, kidneys, liver, lungs, lymph nodes, and spleen of the treated rats. Clearance from the blood, kidneys, and lymph nodes was established by day 14, from the lungs by day 21, and from the liver and spleen by day 28. Given the test results, *S. lydicus* WYEC 108 was not shown to be toxic, infective, or pathogenic to rats.

d. Primary Dermal Irritation (MRID 451117-05; OPPTS Guideline 870.2500)

Three male rabbits were given a single dose of 0.5 g of formulated (end use product) *Streptomyces lydicus* WYEC 108 applied under a gauze pad (MRID# 451117-05; BPPD Data Evaluation Report, dated October 15, 2001). None of the rabbits died during the study and one rabbit had very slight erythema that cleared within 24 hours. The study was originally rated "supplemental" due to questions about the test material (BPPD review - October 15, 2001). The registrant addressed the questions in a letter dated February 28, 2002 and the study was subsequently upgraded to "acceptable" (BPPD Review dated May 21, 2003). With a primary

irritation index of 0.1, the pesticide is considered to be essentially non-irritating and is classified as Toxicity Category IV for primary dermal irritation.

e. Primary Eye Irritation (MRID 451117-04; OPPTS Guideline 870.2400)

Three male rabbits were given a single dose of 0.1 g of formulated (end use product) *Streptomyces lydicus* WYEC 108 applied to the right eye (MRID# 451117-04; BPPD Data Evaluation Report, dated October 15, 2001). None of the rabbits died during the study and no corneal opacity or iritis was noted for any rabbit. All rabbits had positive conjunctival irritation that was resolved or reduced by 24 hours. All irritation was resolved within 72 hours. The study was originally rated "supplemental" due to questions about the test material (BPPD review - October 15, 2001). The registrant addressed the questions in a letter dated February 28, 2002 and the study was subsequently upgraded to "acceptable" (BPPD Review dated May 21, 2003). Given the study results, the pesticide is considered to be minimally irritating and is classified as Toxicity Category IV for primary eye irritation.

f. Hypersensitivity Incidents (OPPTS Guideline 885.3400)

The registrant has reported that there have been no hypersensitivity incidents during production and testing of *Streptomyces lydicus* WYEC 108 (TGAI and formulated end use product) (BPPD Review dated May 21, 2003). However, the registrant must report to the Agency any future incident(s) of hypersensitivity with *Streptomyces lydicus* WYEC 108 under FIFRA Section 6(a)(2).

g. Data Waiver Requests: Health Effects

Data waivers were requested for the following Tier I studies:

(i) Acute Oral Toxicity/Pathogenicity (OPPTS 885.3050)
(ii) Acute Dermal Toxicity/Pathogenicity (OPPTS 885.3100)
(iii) Acute Inhalation Toxicity (OPPTS 870.1300)
(iv) Hypersensitivity Study (OPPTS 870.2600)
(v) Immune Response (Guideline 152-38)

The Agency decided that the justifications provided by the applicant to waive the studies listed above, [(i) through (v)], were acceptable as discussed below [BPPD review of Data Waiver Requests, dated May 21, 2003 (hereinafter referred to as "BPPD Review - May 21, 2003)].

Summaries of discussions for Data Waiver Requests

(i) Acute Oral Toxicity/Pathogenicity (OPPTS 885.3050)

An acceptable acute oral toxicity study (870.1100) was submitted by the registrant (discussed in Part a above). This study showed no mortality or abnormalities among the orally-dosed rats (Toxicity Category IV). In addition, toxicity/pathogenicity studies were conducted on the most likely route of human exposure, pulmonary, and the most sensitive route of exposure, intravenous injection, to determine whether or not the material is toxic, pathogenic, or infective to mammals. Both of those studies were acceptable and demonstrated a lack of toxicity and pathogenicity from *Streptomyces lydicus* WYEC 108 to the test animals. Therefore, the data waiver request for acute oral toxicity/pathogenicity testing is granted (BPPD Review - May 21, 2003).

(ii) Acute Dermal Toxicity/Pathogenicity (OPPTS 885.3100)

The registrant has submitted acceptable acute oral toxicity, acute pulmonary toxicity/pathogenicity, acute injection toxicity/pathogenicity, primary eye irritation, and primary dermal irritation studies that demonstrate the lack of toxicity, pathogenicity, infectivity, and irritation for the active ingredient, *Streptomyces lydicus* WYEC 108 (see discussions above). As such, the data waiver request for acute dermal toxicity/pathogenicity testing is granted (BPPD Review of Dermal Toxicity Data Waiver Request, dated February 11, 2004).

(iii) Acute Inhalation Toxicity (OPPTS 870.1300)

The registrant submitted an acceptable acute pulmonary toxicity/pathogenicity study (see discussion above) that demonstrated no toxicity, pathogenicity, or infectivity associated with the active ingredient, *Streptomyces lydicus* WYEC 108. The inert ingredients in the end-use product are not expected to increase the pathogenicity or toxicity of the TGAI. As such, the data waiver request for acute inhalation toxicity testing is granted (BPPD Review - May 21, 2003).

(iv) Hypersensitivity Study (OPPTS 870.2600)

The registrant has reported that there have been no hypersensitivity incidents during production and testing of *Streptomyces lydicus* WYEC 108 (TGAI or end use product). In addition, the submitted toxicity and irritation studies (as discussed above) have shown minimal toxicity and/or irritation potential for *Streptomyces lydicus* WYEC 108. The registrant will also report any adverse incidents to the Agency under FIFRA section 6(a)(2). Therefore, the data waiver request for the hypersensitivity study is granted (BPPD Review - May 21, 2003).

(v) Immune response (OPPTS 885.3800)

The submitted acute injection toxicity/pathogenicity study (as discussed above) demonstrated that *Streptomyces lydicus* WYEC 108 is cleared by the immune system from the

bodies of the test animals. Therefore, the data waiver request for immune response testing is granted (BPPD Review - May 21, 2003).

Table 2b: Tier I - Data Waivers: Acute Mammalian Toxicity of *S. lydicus* WYEC 108

Guideline	Study	Toxicity Category	Comments	MRID No.
152-30 *885.3050	Acute oral toxicity/ pathogenicity	N/A	Waived** No toxicity observed with Acute oral toxicity study as discussed above.	N/A
152-31 *885.3200	Acute dermal toxicity/ pathogenicity	N/A	Waived** No dermal toxicity/pathogenicity is expected based on submitted toxicity and irritation studies.	N/A
152-32 *870.1300	Acute inhalation toxicity	N/A	Waived** No toxicity/pathogenicity observed in Acute pulmonary toxicity/pathogenicity study as discussed above.	N/A
152-36 *870.2600	Hypersensitivity Study	N/A	Waived** No hypersensitivity incidents have been reported during production/testing of active ingredient. No toxicity or irritation is expected based on submitted data as discussed above.	N/A
152-38 *870.2500	Immune Response	N/A	Waived** Acute injection toxicity/ pathogenicity study showed that the active ingredient is cleared from the body by the immune system.	N/A

***OPPTS Harmonized Guideline Numbers. ** Justifications acceptable, see text.**

f. Subchronic, Chronic Toxicity and Oncogenicity

Based on the data generated in accordance with the Tier I data requirements (40 CFR §158.740(c)), Tier II tests (Guidelines 152B-40 through 152B-49) involving acute oral, acute inhalation, subchronic oral, acute intraperitoneal/intracerebral, primary dermal, primary eye, immune response, teratogenicity, virulence enhancement, and mammalian mutagenicity were not required. As a result, Tier III tests (Guidelines 152-50 through 53) involving chronic testing, oncogenicity testing, mutagenicity, and teratogenicity also were not required.

g. Effects on the Immune and Endocrine Systems

EPA is required under the FFDCA, as amended by FQPA, to develop a screening program to determine whether certain substances (including all pesticide active and other ingredients) "may have an effect in humans that is similar to an effect produced by a naturally-occurring estrogen, or other such endocrine effects as the Administrator may designate." Following the recommendations of its Endocrine Disruptor Screening and Testing Advisory Committee (EDSTAC), EPA determined that there was scientific basis for including, as part of the program, the androgen and thyroid systems, in addition to the estrogen hormone system. EPA also adopted EDSTAC's recommendation that the program include evaluations of potential effects in wildlife. For pesticide chemicals, EPA will use FIFRA and, to the extent that effects in wildlife may help determine whether a substance may have an effect in humans, FFDCA authority to require the wildlife evaluations. As the science develops and resources allow, screening of additional hormone systems may be added to the Endocrine Disruptor Screening Program (EDSP).

The Agency is not requiring information on the endocrine effects of this active ingredient, *Streptomyces lydicus* WYEC 108, at this time. The Agency has considered, among other relevant factors, available information concerning whether the microorganism may have an effect in humans similar to an effect produced by a naturally occurring estrogen or other endocrine effects. There is no known metabolite produced by this microorganism that acts as an "endocrine disrupter". The submitted toxicity/pathogenicity studies in the rodent (required for microbial pesticides) indicate that following injection and pulmonary routes of exposure, the immune system is still intact and able to process and clear the active ingredient. In addition, based on the low potential exposure level associated with the proposed use of this pesticide, the Agency expects no incremental adverse effects to the endocrine or immune systems.

3. Dietary Exposure and Risk Characterization

The method of application for *Streptomyces lydicus* WYEC 108 is a soil mix/drench to

potted plants and turf grass or as a foliar application to greenhouse crops. As such, there may be plant residues of *S. lydicus* WYEC 108 and dietary exposure on agricultural commodities. However, negligible to no risk is expected for the general population, including infants and children, because in the studies submitted in support of the registration, *S. lydicus* WYEC 108 demonstrated no infectivity, pathogenicity, or toxicity potential at the maximum doses tested. Based on the acute oral toxicity study, the pesticide is classified as Toxicity Category IV for oral exposure (BPPD Review - October 15, 2001). A LD_{50} greater than 5050 mg/kg body weight in the acute oral study indicates that consumption of food commodities treated with *S. lydicus* WYEC 108 poses no incremental risk via dietary exposure. Therefore, the Agency has determined that dietary exposure to *S. lydicus* WYEC 108 is not likely to result in any undue health effects or risk. In addition, dietary exposure via drinking water, as presented below (see Section III.B.5 below), does not pose an incremental risk.

4. Occupational and Residential Exposure and Risk Characterization

a. Non-occupational Residential, School and Day Care Exposure and Risk Characterization

Based on the proposed agricultural and horticultural use patterns, the potential for non-dietary exposure to *Streptomyces lydicus* WYEC 108 residues for general population, including infants and children, is unlikely. Accordingly, the Agency believes that the potential aggregate non-occupational exposure, derived from dermal and inhalation exposure from the application of *S. lydicus* WYEC 108 should fall well below the currently tested microbial safety standards.

The potential for dermal or inhalation exposure to *S. lydicus* WYEC 108 pesticide residues for the general population, including infants and children, is unlikely because the potential use sites are agricultural and horticultural. However, since *S. lydicus* WYEC 108 is a common, naturally-occurring soil bacterium, there is a great likelihood of prior exposure for most, if not all individuals. Accordingly, the increase in exposure due to this proposed microbial pesticide would be negligible. Furthermore, as demonstrated by studies submitted in support of the registration (see Section III.B.2 above), the organism is non-pathogenic, non-toxic, and is essentially non-irritating (Toxicity Category IV). As such, the risks anticipated for dermal and inhalation routes of exposure are considered minimal.

b. Occupational Exposure and Risk

Potential exposure of *Streptomyces lydicus* WYEC 108 to workers and pesticide handlers is not expected to pose any undue risk. Pesticide drift is minimized because the end use product is only applied outdoors as a soil drench and is not applied aerially. Foliar applications are for greenhouse use only. Appropriate Personal Protective Equipment (PPE) and a Restricted Entry Interval (REI) of 4 hours for foliar greenhouse applications are required to mitigate any potential

risks to workers and pesticide handlers. PPE for workers and handlers consists of long-sleeved shirt, long pants, shoes, socks, waterproof gloves, and a filtering respirator. Early entry workers must wear coveralls in addition to the PPE above during the REI to perform post-application activities.

The primary routes of exposure for mixer/loaders and applicators would be dermal exposure and/or inhalation. The acute pulmonary toxicity/pathogenicity study submitted in support of the registration demonstrated that *S. lydicus* WYEC 108 is not toxic, pathogenic, or infective. The primary dermal irritation study showed that *S. lydicus* WYEC 108 is essentially non-irritating (Toxicity Category IV). As such, the risks anticipated for occupational exposure are considered minimal.

5. Drinking Water Exposure and Risk Characterization

Exposure to *Streptomyces lydicus* WYEC 108 via drinking water is not likely to be greater than current/existing exposures. *S. lydicus* WYEC 108 is found naturally, but does not thrive in aquatic environments. There are also no aquatic use sites for the pesticide, so exposure in drinking water is not expected. In addition, there is no evidence of adverse effects from oral, dermal, or inhalation exposure to this microbial agent (see Section III.B.2 above). Potential risks via exposure to drinking water or runoff are also adequately mitigated by, among other things, percolation through soil. Thus, exposure from the proposed use of *S. lydicus* WYEC 108 is not likely to pose any incremental risk via drinking water to adult humans, infants and children.

6. Acute and Chronic Dietary Risks for Sensitive Subpopulations Particularly Infants and Children

The method of application for *Streptomyces lydicus* WYEC 108 is a soil mix/drench to potted plants and turf grass or as a foliar application to greenhouse crops. As such, there may be plant residues of *S. lydicus* WYEC 108 and dietary exposure on agricultural commodities. However, negligible to no risk is expected for the general population, including infants and children, because in the studies submitted in support of the registration, *S. lydicus* WYEC 108 demonstrated no pathogenicity or toxicity potential at the maximum doses tested. Based on the acute oral toxicity study, the pesticide is classified as Toxicity Category IV for oral exposure (BPPD Review - October 15, 2001). A LD_{50} greater than 5050 mg/kg body weight in the acute oral study indicates that consumption of food commodities treated with *S. lydicus* WYEC 108 poses no incremental risk via dietary exposure. In addition, dietary exposure via drinking water, as presented above (see Section III.B.5), does not pose an incremental risk. Therefore, the Agency has decided that the acute and chronic risks posed by dietary exposure to the pesticide via proposed use on greenhouse crops are likely to be minimal to non-existent.

7. Aggregate Exposure from Multiple Routes Including Dermal, Oral, and Inhalation

Dermal

Non-occupational dermal exposure and risk are likely to be minimal to non-existent based on:

(i) the potential use sites, which are agricultural and horticultural;
(ii) the application methods, which include use as a soil drench or in greenhouses;
(iii) the lack of dermal irritation demonstrated in the Primary Dermal Irritation study (see Section 2 above);
(iv) the lack of reported hypersensitivity incidents; and
(v) *Streptomyces lydicus* WYEC 108 is a naturally-occurring soil bacterium and there is a great likelihood of prior exposure for most individuals.

Occupational dermal exposure to *Streptomyces lydicus* WYEC 108 has been previously discussed and appropriate measures, such as PPE and REIs, are required to mitigate any potential occupational dermal exposure and risk (see Section III.B.4).

Oral

Oral exposure would occur primarily from eating treated produce. However, negligible to no risk is expected because in the submitted acute oral toxicity study, *Streptomyces lydicus* WYEC 108 demonstrated no pathogenicity or toxicity potential at the maximum doses tested. Based on the acute oral toxicity study, the pesticide is classified as Toxicity Category IV for oral exposure (BPPD Review - October 15, 2001). A LD_{50} greater than 5050 mg/kg body weight in the acute oral study indicates that consumption of food commodities treated with *S. lydicus* WYEC 108 poses no incremental risk via dietary exposure (for more discussion, see Section III.B.3).

Inhalation

The potential for non-occupational inhalation exposure to *Streptomyces lydicus* WYEC 108 pesticide residues is unlikely because the potential use sites are agricultural and horticultural. The greatest occupational inhalation exposure would occur to mixer/loaders and applicators. However, since *S. lydicus* WYEC 108 is a common, naturally-occurring soil bacterium, there is a great likelihood of prior exposure for most, if not all individuals. Accordingly, the increase in exposure due to this proposed microbial pesticide would be negligible. Furthermore, as demonstrated in the acute pulmonary toxicity/pathogenicity test, *S.*

lydicus WYEC 108 demonstrated no infectivity, pathogenicity, or toxicity. Because of the microbial nature of the active ingredient, the Agency has also required that all occupationally exposed workers wear a dust/mist filtering respirator. As such, the risks anticipated for inhalation exposure are considered minimal.

In summary, the potential aggregate exposure, derived from (a) dietary exposure from treated food/feed commodities and from drinking water potentially exposed secondary to treatment of sites with this pesticide, and (b) dermal and inhalation non-occupational and occupational exposure of populations to *Streptomyces lydicus* WYEC 108, is not expected or should be adequately mitigated, as long as the pesticide is used as labeled.

8. Cumulative Effects

Section 408(b)(2)(D)(v) of the FFDCA requires the Agency to consider the cumulative effect of exposure to *Streptomyces lydicus* WYEC 108 and to other substances that have a common mechanism of toxicity. These considerations include the possible cumulative effects of such residues on infants and children. The Agency has considered the potential for cumulative effects of *S. lydicus* WYEC 108 and other substances in relation to a common mechanism of toxicity. These considerations include the possible cumulative effects of such residues on infants and children. As demonstrated in Section III.B.2 above, *S. lydicus* WYEC 108 is non-toxic and non-pathogenic to mammals. Because no mechanism of pathogenicity or toxicity in mammals has been identified for this organism, no cumulative effects from the residues of this product with other related microbial pesticides are anticipated.

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

There is a reasonable certainty that no harm to the U.S. population, including infants and children, will result from aggregate exposure to residues of *Streptomyces lydicus* WYEC 108 due to its use as a microbial pest control agent. This includes all anticipated dietary exposures and all other exposures for which there is reliable information. As discussed in Unit III above, *S. lydicus* WYEC 108 is not pathogenic or infective and is non-toxic to mammals. Accordingly, exempting *S. lydicus* WYEC 108 from the requirement of a tolerance should be considered safe and pose no significant risks.

FFDCA section 408(b)(2)(C) provides that EPA shall apply an additional tenfold margin of exposure (safety) for infants and children in the case of threshold effects to account for prenatal and postnatal toxicity and the completeness of the database on toxicity and exposure, unless EPA determines that a different margin of exposure (safety) will be safe for infants and children. Margins of exposure (safety) are incorporated into EPA risk assessment 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. Because *S. lydicus* WYEC 108 is a common, naturally-occurring bacterium, residues of this microbial pesticide in or on agricultural commodities are not expected to significantly increase exposure to the U.S. population, including infants and children. In addition, actual exposures to adults and children through diet are expected to be several orders of magnitude less than the doses used in the toxicity and pathogenicity tests referenced in Section III.B.2 above. EPA concludes that the toxicity and exposure data are sufficiently complete to adequately address the potential for additional sensitivity of infants and children to residues of *S. lydicus* WYEC 108. Therefore, there is a reasonable certainty that no harm will result to infants and children from aggregate exposure to *S. lydicus* WYEC 108 residues.

C. Environmental Assessment

1. Ecological Effects Hazard Assessment

Below is a summary of the ecological effects database evaluated in support of this action. The database for studies and information of toxicity of *Streptomyces lydicus* WYEC 108 to non-target organisms are sufficient to allow unconditional registration as a microbial pesticide for use on agricultural and horticultural use sites.

a. Toxicity to Non-target Animals

(i) Freshwater Fish Testing (MRID 451117-06, OPPTS 885.4200; Gdln 154 -19)

The potential toxicity of *Streptomyces lydicus* WYEC 108 to rainbow trout was assessed in an acute toxicity test. Trout were exposed to five concentrations of the active ingredient (and a negative control) and observed for a 96 hour period. No mortality or observations of toxicity or abnormal behavior were shown. The 96 hour LC_{50} for rainbow trout exposed to *S. lydicus* WYEC 108 was determined to be >167 µg/L (>1.0 x 10^6 CFU/ml). The 96 hour NOEC for *S. lydicus* WYEC 108 was determined to be 167 µg /L (MRID# 451117-06; BPPD Data Evaluation Report, dated May 25, 2001).

Table 3a: Eco-Toxicology Summary/Studies Evaluated

Guideline No.	Study	Status, Classification & Comments	MRID Nos.
154-19 *885.4200	Freshwater fish testing	Acceptable. No mortality or observations of toxicity or abnormal behavior were shown. The LC_{50} for rainbow trout exposed to *S. lydicus* WYEC 108 was determined to be >167 µg/L (>1.0 x 10^6 CFU/ml).	451117-06

*885 series = OPPTS Microbial Pesticide Test Guideline Numbers.

b. Data Waivers: Ecological Effects

The following ecological effects studies were waived:
(i) Avian oral toxicity (OPPTS 885.4050; Gdln 154-16)
(ii) Wild Mammal Testing (OPPTS 885.4150; Gdln. 154A-18)
(iii) Freshwater Aquatic Invertebrate Testing (OPPTS 885.4240; Gdln 154-20)
(iv) Estuarine and Marine Animal testing (OPPTS 885.4280; Gdln 154-21)
(v) Non-target Plant studies (OPPTS 885.4300; Gdln 154-22)
(vi) Non-target Insect testing (OPPTS 885.4340; Gdln 154-23)

Justifications for data waivers

Rationales for these data waiver requests are summarized below:

(i) Avian Oral Toxicity (OPPTS 885.4050; Gdln 154-16)

The registrant submitted a waiver request for avian oral toxicity testing based on the following rationale: 1) the concentration of *Streptomyces lydicus* in soil resulting from application of the end product is similar to, or lower than, the maximum levels that occur during the normal growth cycle, 2) there is a lack of infectivity of *Streptomyces lydicus* to animals in the laboratory and insects in the natural environment, and 3) there is a lack of toxicity of the antibiotic extract from *Streptomyces lydicus* in birds.

The Agency review of the waiver request determined that the proposed use patterns would result in little exposure to avian species orally and if exposure did occur, it would be at levels near or lower than natural *Streptomycete* populations. In addition, the submitted Acute Injection Toxicity/Pathogenicity study (see section III.B.2 above), there were no mortalities at a dose of 9.33×10^8 CFU/animal and injected *S. lydicus* WYEC 108 cleared from various tissues in 3 - 28 days. It is unlikely, given the above evidence, that toxicity or pathogenicity from *S. lydicus* WYEC 108 or the inerts in the end product would occur. As such, the waiver request for avian oral toxicity testing is granted (BPPD Review - May 21, 2003).

(ii) Avian Injection/Inhalation Testing (OPPTS 885.4100; Gdln 154-17)

The registrant submitted a waiver for the avian injection/inhalation study due to the lack of toxicity of the antibiotic extract from *Streptomyces lydicus* to birds, the lack of infectivity to animals in the laboratory and the lack of infectivity to insects in the environment.

The Agency review of the waiver noted that *Streptomyces* species do not commonly infect animals, which is confirmed by the Manual of Clinical Microbiology (2003); 8th edition.

There were no data or literature citations given to support the claim that *Streptomyces lydicus* WYEC 108 will not infect non-target insects and otherwise provide significant exposure to birds. However, EPA finds little opportunity for broad exposure of insects or birds to *Streptomyces lydicus* WYEC 108 given the proposed label use patterns: on Greenhouse and Nursery plants and as a soil drench on turf grass. The proposed use patterns are expected to result in *Streptomyces lydicus* WYEC 108 in the soil at levels (claimed 10^6 CFU/g) that are below natural *Streptomycete* levels (10^{7-8} CFU/g), with smaller, background amounts expected in air and on plant surfaces. Therefore, the waiver request for avian injection/inhalation testing is granted (BPPD Review - May 21, 2003).

(iii) Wild Mammal Testing (OPPTS 885.4150; Gdln. 154A-18)

The registrant has requested a waiver for wild mammal testing due to the proposed use patterns, expected to result in *Streptomyces lydicus* WYEC 108 in the soil at levels (claimed 10^6 CFU/g) that are below *Streptomycete* levels (10^{7-8} CFU/g) found naturally, with smaller background amounts expected in air and on plant surfaces.

Based on the lack of observed mammalian toxicity/pathogenicity effects (see section III.B.2), the Agency has decided that the use of *Streptomyces lydicus* WYEC 108 as a pesticide is not likely to pose incremental hazards to wild mammals, if it is used as labeled. No additional testing at higher tiers is ordinarily required, since no pathogenic effects were observed in the mammalian studies. In addition, EPA notes that *Streptomyces* species do not commonly infect animals, which is confirmed by the Manual of Clinical Microbiology (2003); 8th edition. Therefore, the waiver request for wild mammal testing is granted (BPPD Review - May 21, 2003).

(iv) Freshwater Aquatic Invertebrate Testing (OPPTS 885.4240; Gdln. 154-20) and Estuarine and Marine Animal Testing (OPPTS 885.4280; Gdln. 154-21)

The registrant requested a waiver for freshwater aquatic invertebrate and estuarine and marine animal testing due to the claim that *Streptomyces lydicus* is specific to soil rather than water, and due to the lack of animal infectivity demonstrated by *S. lydicus* and closely related microbes. One citation was given: Moran, MA, LT Rutherford and RE Hodson. 1995. Evidence for indigenous *Streptomyces* populations in a marine environment determined with a 16S rRNA probe. Appl Environ Microbiol 61(10): p. 3695-3700.

EPA interpretation is that the *Streptomyces* populations in this citation freely lived in marine sediment and were not incidental from soil runoff. No reported attempt was made to differentiate live organisms in marine sediment or compare them to *Streptomyces* found in agricultural soils.

Data presented for this waiver request show die-off of *Streptomyces lydicus* WYEC 108 during exposure of Rainbow Trout in a static system at the lowest dose: 5.65 x 10^3 CFU/mL at start, 2.8 x 10^3 CFU/mL at 48 hours (50 % of start) and 4.95 x 10^2 CFU/mL after 96 hours (8.8 % of start). At the highest dose, the population of *Streptomyces lydicus* WYEC 108 declined to 18 % of start by 96 hours. The registrant notes that application to water, or wash-off of product into water, at an application rate of 1 x 10^6 CFU/g, is expected to decrease by half in 2 days since *Streptomyces lydicus* WYEC 108 is not adapted to fresh water.

EPA considered that while *Streptomyces lydicus* WYEC 108 is not adapted to water, survival and growth in sediment may occur. The conclusions regarding no effect to all aquatic species in estuarine and marine environments are not founded given a reference involving marine sediment, and the 96-hour acute toxicity study to Rainbow Trout. Effects caused by pathogenicity or toxicity often emerge after infection and growth of an organism so an applicable test for Microbial Pest Control Agent (MPCA) toxicity / pathogenicity to Freshwater Fish would have been OPPTS Guideline 885.4200, a 30-day (or longer) test. However, due to the proposed use patterns, i.e. Greenhouses and Nurseries, and on turf grass, exposure to aquatic organisms by *S. lydicus* WYEC 108 is not expected at high levels. The registrant noted that *Streptomyces* species do not commonly infect animals, which is confirmed by the Manual of Clinical Microbiology (2003); 8th edition. Based on this information, the registrant request to waive freshwater aquatic invertebrate and estuarine and marine animal testing is granted (BPPD Review - May 21, 2003).

(v) Non-target Plant studies (OPPTS 885.4300; Gdln. 154-22)

The registrant requested a waiver for non-target plant testing, claiming: 1) there is lack of plant infectivity by *Streptomyces lydicus* WYEC 108 in laboratory studies, and 2) *Streptomyces lydicus* is ubiquitous in soils worldwide with a lack of plant infectivity. *Several literature citations characterizing plant interactions with Streptomyces lydicus were cited in support of the waiver request: 1)* Yuan, WM and DL Crawford. 1995. Characterization of *Streptomyces lydicus* WYEC108 as a potential biocontrol agent against fungal root and seed rots. Appl Envir Microb, 61(8): p.3119-28; and 2) Tokala, RK, JL Strap, CM Jung, DL Crawford, MH Salove, LA Deobald, JF Bailey and MJ Morra. 2002. Novel plant-microbe rhizosphere interaction involving *Streptomyces lydicus* WYEC108 and the pea plant (*Pisum sativum*). Appl Environ Microbiol 68(5): p.2161-71. The registrant also noted that two *Streptomycetes*, *Streptomyces ipomoea* and *Streptomyces scabies*, cause soil rot on sweet potato and scab on potato, respectively.

The Agency review noted that there is no immediately available evidence of plant diseases, other than literature cited in the waiver request, caused by *Streptomycetes* (Science Direct, Agricola, Current Contents) and USDA-APHIS does not list any *Streptomycete* on it's Regulated Plant Pest List (6/16/00). The registrant claims that data submitted to USDA from

studies at the University of Idaho show no adverse effects to potato by *Streptomyces lydicus* WYEC 108. These data were not submitted to EPA. EPA agrees that nontarget plant testing to support registration of Actinovate™ Soluble (end use product) for the current label uses is not necessary and the waiver request is granted. *However,* if future uses include potato or sweet potato crops, definitive plant pathogenicity test data should be submitted for review (BPPD Review - May 21, 2003).

(vi) Non-target Insect testing (OPPTS 885.4340; Gdln. 154-23)

The registrant requested a waiver for non-target insect testing based on the ubiquitous distribution of *Streptomyces* species throughout the world, with an assumed constant non-target insect exposure. *The* EPA review noted that *Streptomyces* species do not commonly infect animals, which is confirmed by the Manual of Clinical Microbiology (2003); 8th edition. There were no data or literature citations included to support the claim that *Streptomyces lydicus* WYEC 108 will not infect non-target insects. However, EPA finds little opportunity for broad exposure of non-target insects to *S. lydicus* WYEC 108 given the proposed label use patterns: on Greenhouse and Nursery plants and as a soil drench on turf grass. The proposed use patterns are expected to result in *Streptomyces lydicus* WYEC 108 in the soil at levels (claimed 10^6 CFU/g) that are below natural *Streptomycete* levels (10^{7-8} CFU/g), with smaller, background amounts expected in air and on plant surfaces. *As such, the waiver request for non-target insect testing is granted (BPPD Review - May 21, 2003).*

(vii) Honey Bee Testing (OPPTS 885.4380; Gdln 154-24)

The registrant requested a waiver for honey bee testing based on the ubiquitous distribution of *Streptomyces lydicus* throughout the world, and the presumed natural exposure to Honey Bees with no reported adverse effects. Expected application rates of *Streptomyces lydicus* WYEC 108 at 10^6 CFU/g would still be below natural levels of 10^{7-8} CFU/g soil and though foliar exposures would occur, significant exposures by this route would be unlikely and at low levels.

The Agency review noted that there are no *Streptomycete*-related microbes commonly reported that cause bee diseases. Expected exposure of bees to *Streptomyces lydicus* WYEC 108 on foliage with the current proposed use patterns would be minimal. Therefore, the waiver request for honey bee testing is granted (BPPD Review - May 21, 2003).

Table 3b: Eco-Toxicology Summary: Data Waivers

Guideline No.	Study	Status, Classification & Comments	MRID Nos. Reviewed
154-16 *885.4050	Avian oral toxicity	Waived** Little or no exposure expected for avian species. Active ingredient is not toxic, infective, or pathogenic (shown in Section III.B) and is not known to infect animals.	N/A
154-17 *885.4100	Avian injection/ inhalation testing		
154-18 *885.4150	Wild mammal testing	Waived** No toxic, infective, or pathogenic effects were observed in the mammalian toxicity tests (as shown in Section III.B) and the active ingredient is not known to infect animals.	N/A
154-20 *885.4240	Freshwater aquatic invertebrate testing	Waived** *S. lydicus* is not known to thrive in water although it may live in marine sediments. However, due to the proposed use patterns (greenhouses, nurseries, and turf grass), exposure to aquatic organisms is not expected at high levels. Also, the active ingredient is not known to infect animals.	N/A
154-21 *885.4280	Estuarine and marine animal testing		
154-22 *885.4300	Non-target plant studies	Waived** There is no available evidence that the active ingredient causes plant diseases. However, other *Streptomycetes* are known to cause diseases in potato and sweet potato. If future uses of *S. lydicus* WYEC 108 include potato and sweet potato crops, definitive plant pathogenicity test data should be submitted for review.	N/A
154-23 *885.4340	Non-target insect testing	Waived** The active ingredient is not known to infect animals and the proposed uses (greenhouses, nurseries, and turf grass) offer little opportunity for broad exposure to non-target insects.	N/A

154-24 *885.4380	Honey bee testing	Waived** there are no *Streptomycete*-related microbes commonly reported that cause bee diseases. Expected exposure of bees on foliage with the current proposed use patterns would be minimal.	N/A

*885 series = OPPTS Microbial Pesticide Test Guideline Numbers.
** Justifications acceptable, see text above for discussion.

2. Environmental Fate, Ecological Exposure, and Environmental Expression Risk Characterization

Streptomyces lydicus WYEC 108 is a ubiquitous and naturally-occurring soil microorganism. As a "free-living" and saprophytic soil organism, *S. lydicus* has not been shown to have a specific fungal host range, yet the organism is readily isolated from soils and plant rhizospheres. The proposed use patterns are expected to result in *S. lydicus* WYEC 108 in the soil at levels (claimed 10^6 CFU/g) that are below natural *Streptomycete* levels (10^{7-8} CFU/g), with smaller, background amounts expected in air and on plant surfaces (BPPD Review - May 21, 2003). This represents a small proportion of the naturally-occurring *Streptomycete*s in the soil and therefore is not expected to add substantially to the effects of the naturally occurring *Streptomycete* populations.

The Agency finds little opportunity for broad exposure of non-target organisms to *Streptomyces lydicus* WYEC 108 given the proposed use sites in greenhouses, nurseries, and on turf grass. Incremental exposures of *S. lydicus* WYEC 108 to the environment and to non-target organisms that inhabit or pass through treated areas do not present an adverse concern as a consequence of the proposed uses of *S. lydicus* WYEC 108. The ecological data and waiver discussions (as summarized above in Section III.C.1 above) support a conclusion of reasonable certainty that no incremental hazards to non-target organisms or to the environment are expected as a result of the intended use of *S. lydicus* WYEC 108.

D. Efficacy Data

Efficacy data were not reviewed by the Agency because the end use product is not labeled for public health pests.

IV. RISK MANAGEMENT AND REGISTRATION DECISION

A. Determination of Eligibility

Section 3(c)(5) of FIFRA provides for the registration of a new active ingredient if it is determined that (A) its composition is such as to warrant the proposed claims for it; (B) its labeling and other materials required to be submitted comply with the requirements of FIFRA; (C) it will perform its intended function without unreasonable adverse effects on the environment; and (D) when used in accordance with widespread and commonly recognized practice, it will not generally cause unreasonable adverse effects on the environment.

To satisfy Criterion "A" above, *Streptomyces lydicus* WYEC 108 has well known properties. The Agency has no knowledge that would contradict the claims made on the label of this product and the active ingredient is not expected to cause unreasonable adverse effects when used according to label instructions. Criterion "B" is satisfied by the current label and by the data presented in this document. It is believed that this new pesticidal active ingredient will not cause any unreasonable adverse effects, and is likely to provide protection as claimed, satisfying Criterion "C". Criterion "D" is satisfied in that *S. lydicus* WYEC 108 is not expected to cause unreasonable adverse effects when used according to label instructions.

Therefore, *S. lydicus* WYEC 108 is eligible for registration. The uses are listed in Table 4, Appendix A.

B. Regulatory Position

1. Unconditional Registration

The data requirements are fulfilled and the Biopesticides and Pollution Prevention Division recommends unconditional registration of products that contain *Streptomyces lydicus* WYEC 108 as a new active ingredient (Actinovate Soluble).

2. Tolerances for Food Uses and /or exemptions

EPA received a pesticide petition (PP 0F6163) from Natural Industries Inc., proposing [pursuant to section 408(d) of the Federal Food, Drug and Cosmetic Act, 21 U.S.C. section 346a(d)], to amend 40 CFR part 180 by establishing an exemption from the requirement of a tolerance for residues of the microbial pesticide, *Streptomyces lydicus* WYEC 108, on growing crops.

EPA is issuing a notice establishing an exemption from the requirements of a tolerance for residues of *Streptomyces lydicus* WYEC 108 in or on all food commodities (40 CFR 180.1253).

3. CODEX Harmonization

There are no Codex harmonization considerations since there is no Codex Maximum Residue Limits set for food use of this active ingredient.

4. Non-food Re/Registrations

This is a new active ingredient and, therefore, not the subject of reregistration at this time.

5. Risk Mitigation

There is minimal or negligible potential risk to non-target organisms (plants and wildlife), and to ground and surface water contamination through the proposed use of products containing *Streptomyces lydicus* WYEC 108 as discussed in this document. No mitigation measures are required at this time for dietary risk, including risk due to exposure via drinking water. Appropriate PPE is required for pesticide handlers. These include long-sleeved shirt, long pants, shoes plus socks, and a dust/mist filtering respirator. The product label will also bear Environmental Hazards text to mitigate any potential risk as determined by reviewed data and use sites.

6. Endangered Species Statement

Currently, the Agency is developing a program (The Endangered Species Protection Program) to identify all pesticides whose use may cause potential adverse impacts on endangered and threatened species and their habitats. To aid in the identification of threatened and endangered species and their habitats, several companies have formed an Endangered Species Task Force (EST) under the direction of the American Crop Protection Association (ACPA). Moreover, the EST will assist in providing species location information at the subcounty level, and, particularly, if an endangered species occurs in areas where pesticides would be used. This information will be useful once the Endangered Species Protection Program has been implemented.

Based on the submitted data (as discussed in section III), *Streptomyces lydicus* WYEC 108 is not known to be toxic or pathogenic and is not known to infect animals or cause plant diseases. Therefore, the Agency has made a no effect finding for the proposed uses of

Streptomyces lydicus WYEC 108. Thus, no labeling is required for endangered species at this time.

C. LABELING RATIONALE

1. End-use Product Labeling

It is the Agency's position that the labeling for End-use products containing *Streptomyces lydicus* WYEC 108 must comply with the pesticide labeling requirements in existence when such products are registered.

a. Human Health Hazard

(i) Worker Protection Standard

Any product whose labeling reasonably permits use in the production of an agricultural plant on any farm, forest, nursery, or greenhouse must comply with PR Notice 93-7, "Labeling Revisions required by the Worker Protection Standard (WPS), and PR Notice 93-11, "Supplemental Guidance for PR Notice 93-7", which reflect the WPS (40 CFR part 156, subpart K). These labeling revisions are necessary to implement the Worker Protection Standard for Agricultural Pesticides (40 CFR part 170). Unless specifically directed otherwise, all statements required by PR Notices 93-7 and 93-11 are to be on the product label exactly as instructed in those Notices.

The labels and labeling of all products must comply with EPA's current regulations and requirements as specified in 40 CFR 156.10 and other applicable notices, such as, and including the WPS labeling. *Streptomyces lydicus* WYEC 108 products with commercial use sites are subject to the Worker Protection Standard. Because of the low toxicity of *S. lydicus* WYEC 108, the Restricted Entry Interval (REI) for greenhouse foliar applications within the scope of WPS is four hours. For use as a soil amendment (incorporation into soil mixes), the REI is zero hours due to the low likelihood of contact with treatment residues. Precautionary statements and personal protective equipment (PPE) as specified below are required based on the acute toxicity categories of this organism.

Workers and handlers (including mixer/loaders and applicators) applying this product must wear long-sleeved shirt, long pants, shoes plus socks, and a dust/mist filtering respirator meeting NIOSH standards of at least N-95, R-95, or P-95. Post application agricultural workers and early-entry workers must wear coveralls in addition to the PPE above when entering treated areas during the REI period of four hours.

(ii) Non-Worker Protection Standard

For non-WPS uses of *Streptomyces lydicus* WYEC 108, unprotected persons must stay out of treated areas until the sprays have dried or the dusts have settled.

(iii) Other Precautionary Labeling

The Agency has examined the toxicological data base for *Streptomyces lydicus* WYEC 108 and concluded that the precautionary labeling required (i.e. Signal Word, First Aid Statements, WPS statements for pesticide handlers, and other label statements) adequately mitigates the risks associated with the proposed uses. Additional labeling may be required for other uses of products containing *Streptomyces lydicus* WYEC 108 on a case-by-case basis.

b. Environmental Hazards Labeling

Provided the following statements are placed in the environmental hazards statement, the risk of exposure to *Streptomyces lydicus* WYEC 108 is minimal to nonexistent to non-target organisms including endangered species:

> "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 rinsate or equipment washwaters."

2. Application Rate

It is the Agency's position that the labeling for the pesticide products containing *Streptomyces lydicus* WYEC 108 must comply with the current pesticide labeling requirements. The pesticide is to be applied as a soil mix/drench to potted plants, to turf grass, or to plant foliage in greenhouses. Application rates for soil mix are 6 oz. end product per 100 gallons water (1 gallon solution into 1 cubic foot of soil mix). For turf grass, the rate is 52 oz. dissolved end product per acre (initial application) and 18 oz. per acre (maintenance treatments). Rates for foliar application (greenhouse) are 6-12 oz. end product dissolved in water per acre. The Agency has not set a maximum number of applications per a season for this active ingredient.

D. LABELING

1. Manufacturing Use Product

There is no separate manufacturing use product (MP) registered at this time.

2. End-use Product
End-use Product name: Actinovate Soluble

Ingredient Statement:	
Streptomyces lydicus WYEC 108*.....	0.0371 %
Inert Ingredients	99.9629 %
Total	100.0000 %

* End-use Product contains not less than 1 x 10^7 CFU/g

Based on the evaluation of the acute oral and acute pulmonary toxicity/infectivity studies submitted in support of the conditional registration of the product, containing *Streptomyces lydicus* WYEC 108, the signal word is "Caution". Signal words for other end-use products containing this active ingredient will vary depending on the toxicity/pathogenicity evaluations of those products. In addition, the product label shall contain the following information:

- Product Name
- Ingredient Statement
- Registration Number
- "Keep Out of Reach of Children"
- Signal Word (CAUTION)
- First Aid Statement (optional)
- Personal Protective Equipment (PPE) Requirements
- Environmental Hazard Statement
- Storage and Disposal Statement
- Agricultural Use Requirements
- Non-Agricultural Use Requirements
- Directions for Use

V. ACTIONS REQUIRED BY REGISTRANTS

Reports of incidents of adverse effects to humans or domestic animals are required under FIFRA, Section 6(a)(2) and incidents of hypersensitivity under 40 CFR Part 158.690(c), guideline reference number 152-16. There are no data requirements, label changes and other responses necessary for the reregistration of the end-use product since the product is being registered after November 1984 and is, therefore, not subject to reregistration. For the same reason, there are also no existing stocks provisions at this time. Before releasing these products for shipment, the registrant is required to provide appropriate labels and other Agency requirements as discussed in this Biopesticide Registration Action Document.

VI. APPENDICES

APPENDIX A - Use sites

Table 4 lists the use sites for the product. The registrant must comply with the appropriate labeling requirements before releasing products containing *Streptomyces lydicus* WYEC 108 as the active ingredient for shipment.

Table 4: Use Site Unconditional registration

Actinovate Soluble Use Sites greenhouses, nurseries, turf grass, ornamental bulb crops	**Official date registered:**

APPENDIX B - Citations Considered to be part of the database supporting the unconditional registration of *Streptomyces lydicus* WYEC 108.

CITATIONS/BIBLIOGRAPHY

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1. Federal Register: August 1, 2000 (Volume 65, Number 148) (Notices) (Page 46912-46916). *Streptomyces lydicus* WYEC 108; Notice of Filing of Pesticide Petitions to Establish Tolerances for Certain Pesticide Chemicals in or on Food (PP 0F6163).

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BPPD Data Evaluation Records/Reviews

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Carl Etsitty and Roy Sjoblad, U.S. EPA, OPP/BPPD. October 15, 2001. Review of data

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