



**US Environmental Protection Agency**  
**Office of Pesticide Programs**  
**Biopesticide Registration Action Document**  
**for Zucchini Yellow Mosaic**  
**Virus – Weak Strain PV-593**

**August 2007**

# Biopesticide Registration Action Document for Zucchini Yellow Mosaic Virus – Weak Strain PV-593

U.S. Environmental Protection Agency  
Biopesticides and Pollution Prevention Division  
Prepared by Gail S. Tomimatsu, Ph.D.  
August 2007

## TABLE OF CONTENTS

### *Zucchini Yellow Mosaic Virus - Weak Strain* (PC Code 244201)

<b>I. EXECUTIVE SUMMARY/FACT SHEET</b> .....	5
<b>II. OVERVIEW</b> .....	8
<b>A. Product Overview</b> .....	8
<b>B. Use Profile</b> .....	8
<b>C. Estimated Usage</b> .....	8
<b>D. Data Requirements</b> .....	8
<b>E. Regulatory History</b> .....	8
1. Section 3 Registration and Exemption from Tolerance.....	9
<b>III. RISK ASSESSMENT</b> .....	10
<b>A. Physical and Chemical Properties Assessment</b> .....	10
1. Product Identity and Mode of Action.....	10
2. Physical and Chemical Properties Assessment.....	11
<b>B. Human Health Assessment</b> .....	12
1. Toxicological Hazard Assessment.....	12
2. Dietary Exposure Assessment.....	16
a. Food Clearances/Tolerances.....	16
b. Dietary Risk Characterization.....	16
c. Drinking Water Risk Characterization.....	16
d. Acute and Chronic Dietary Risks for Sensitive Subpopulations Particularly Infants and Children.....	16
e. Determination of Safety for U.S. Population, Infants and Children.....	17
f. Aggregate Exposure from Multiple Routes Including Dermal, Oral, and Inhalation....	17
g. Cumulative Effects.....	18
3. Occupational and Residential Risk Characterization.....	18
a. Non-Occupational Residential, School and Day Care Exposure and Risk Characterization.....	18
b. Occupational Exposure and Risk.....	18
<b>C. Environmental Assessment</b> .....	19
1. Ecological Effects Hazard Assessment.....	19

2. Environmental Fate, Ecological Exposure, and Environmental Expression Risk Characterization.....	22
3. Endangered Species Assessment.....	23
<b>D. Efficacy Data</b> .....	24
<b>IV. RISK MANAGEMENT AND REGISTRATION DECISION</b> .....	24
<b>A. Determination of Eligibility</b> .....	24
<b>B. Regulatory Position</b> .....	25
1. Unconditional Registration.....	25
2. Tolerances for Food Uses and/or Exemption.....	25
3. CODEX Harmonization.....	25
4. Non-food Registrations.....	25
5. Risk Mitigation.....	25
<b>C. Use Sites</b> .....	26
<b>D. Labeling</b> .....	26
1. Human Health Hazards.....	26
2. Environmental Hazards.....	27
3. Application Rate.....	27
4. Ingredient Statement.....	27
<b>V. ACTIONS REQUIRED BY REGISTRANTS</b> .....	27
<b>VI. BIBLIOGRAPHY</b> .....	28
<b>A. Studies Submitted in Support of this Registration</b> .....	28
<b>B. Federal Register Publications</b> .....	30
<b>C. BPPD Evaluation Records/Reviews</b> .....	30

**BIOPESTICIDE REGISTRATION ACTION DOCUMENT TEAM**

**Office of Pesticide Programs  
Biopesticides and Pollution Prevention Division  
Microbial Pesticides Branch**

**Health Effects**

Joel Gagliardi  
John Kough

Microbial Ecologist  
Biologist

**Ecological Effects**

Mika Hunter  
Zigfridas Vaituzis

Biologist  
Microbiologist

**Regulations**

Gail Tomimatsu  
Sheryl Reilly

Plant Pathologist  
Branch Chief

## I. EXECUTIVE SUMMARY/FACT SHEET

### Active Ingredient and Proposed Use

The active ingredient, *Zucchini Yellow Mosaic Virus - Weak Strain* (PC Code 244201, ATCC PV-593<sup>1</sup>) (also referred to in this document as *ZYMV-WK*), is a natural variant of the plant virus *Zucchini Yellow Mosaic Virus* (*ZYMV*). The “WK” strain was originally isolated in France in 1986 from an infected melon (*Cucurbita pepo*) branch which showed attenuated (i.e., weakened) *ZYMV* disease symptoms.

*Zucchini Yellow Mosaic Virus - Weak Strain* acts as a cross-protectant to stimulate plant cell post-transcriptional gene silencing (PTGS) reactions to those *ZYMV* strains that cause severe disease symptoms. *ZYMV-WK* replicates in susceptible Cucurbitaceae, but does not cause overt plant disease and is transmitted poorly by aphids. When young plants are inoculated with the active ingredient, *ZYMV-WK*, mild disease symptoms appear only on the leaves (i.e., local lesions leaf mottling, and mosaic pattern); and there are no subsequent fruit malformations.

There is only one product (end-use product = manufacturing use product, AgroGuard™ Z); the active ingredient, *ZYMV-WK* is formulated in homogenized zucchini leaves. This product may be applied only to young plants, with a special apparatus (Bim-GH™; Bim-Field™) to “inject” the pesticide onto the foliage of greenhouse or field transplants before appearance of the 4<sup>th</sup> true leaf, or before transplanting inoculated plants into the field. *ZYMV-WK* has been registered as a pesticide in the European Union and in Israel (Braverman, 2006 MRID # 470083-04). It has been registered as Curbit™ in Israel since 1997 and in the UK since 2006.

### Toxicology, Human Exposure and Risks

Assessments of submitted mammalian waiver rationale 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 on young cucurbit plants. For occupational exposures, the technical grade active ingredient (TGAI) was classified as Toxicity Category III for acute oral toxicity, acute inhalation toxicity, acute dermal toxicity, primary dermal irritation, acute oral toxicity, and primary eye irritation, because all acute toxicity/pathogenicity requirements were fulfilled by acceptable waiver rationale.

The Agency accepted requests to waive acute oral toxicity/pathogenicity, acute dermal toxicity/pathogenicity, acute dermal irritation, primary eye irritation, acute pulmonary toxicity/pathogenicity, acute injection toxicity/pathogenicity, and cell culture guideline testing. The rationale for granting these waivers was based on the biology and ecology of plant viruses, especially of *ZYMV* and *ZYMV-WK*, and the low potential for adverse effects to human health, nontarget organisms, or to the environment. Also, there were no documented reports of hypersensitivity

---

<sup>1</sup> The American Type Culture Collection (ATCC) is an international collection point for microorganisms.

incidents during production, testing and use of the manufacturing use product and the end-use product (i.e., Curbit™) [Table 3b 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 Part 180 for residues of *ZYMV-WK* on all cucurbit commodities when used/applied in accordance with label directions.

#### *FQPA Considerations*

The Agency has considered *ZYMV-WK* in light of the safety factors identified in the Food Quality Protection Act (FQPA) of 1996, and has determined that there is a reasonable certainty of no harm to the U.S. population in general, and to infants and children in particular from the pesticidal use of *ZYMV-WK* in or on food commodities. Humans are exposed to the weak and severe strains of the plant virus, since *ZYMV* and other plant viruses in or on food crops exist as natural infestations. Throughout the available literature, there are no reports of adverse effects in animals resulting from ingestion of, or exposure to plant viruses. In addition, there are no reports of adverse effects in humans that handle and administer the viruses, or of the laboratory animals exposed to this virus developing any nasal, eye, skin, or pulmonary allergic reactions, or any other adverse reactions. Although the plant virus was found in Europe and formulated in Israel, weak strains of plant virus typically co-exist with more severe strains in natural infections and plant disease. Thus, application of *ZYMV-WK* to young cucurbit crops for agricultural purposes is not expected to increase the risks to humans and the environment [Section III.B.3].

Toxicity endpoints which justify setting numerical tolerances for a pesticide product were not identified for the MPCA, *ZYMV-WK*. The OECD Dossier for the UK registration of *ZYMV-WK* contained additional public information regarding plant virus biology and ecology which indicated a low potential for adverse effects to human or mammalian health. Furthermore, routine exposures to farm personnel, consumers and laboratory researchers have not led to any known adverse effects (ill health, sensitization or allergenicity). As a plant virus found primarily on diseased cucurbits, e.g., zucchini, the active ingredient demonstrates no acute oral toxicity potential (Toxicity Category IV) and shows no incremental dietary risk [Section III.B.3]. Therefore no acute, subchronic, chronic, immune, endocrine, or non-dietary exposure issues were identified that would indicate any incremental adverse effects on infants, children, and the general U.S. population. Based on the classification of Toxicity Category IV for acute oral toxicity, a safety factor is not required for residues of *ZYMV-WK*. Potential risks via exposure to drinking water or runoff are not expected, because the plant virus does not occur, or replicate in aquatic environments [Section III.B.5].

The potential for aggregate, non-occupational exposure is unlikely, because use sites identified for the subject active ingredient are agricultural. Pesticide products containing *ZYMV-WK* will be applied as a directed spray to young cucurbit plants in semi-enclosed environments, or to young plants in fields

early in the crop season. If such exposure occurred, the risk concerns would be negligible, since the plant virus is not a human pathogen, and is not toxic to mammals.

### **Occupational and Residential Exposure and Risk**

Occupational exposure to ZYMV-WK is not anticipated; however, in order to mitigate exposures to pesticide handlers/applicators and agricultural workers, any pesticide product containing this active ingredient should bear the appropriate Personal Protective Equipment (PPE) for agricultural applications. Residential exposure is not expected since the end use products will be intended for use in agricultural settings. Risk to workers, pesticide handlers, and residential communities are very low since the TGAI is minimally toxic and non-pathogenic to mammals.

### **Ecological and Environmental Exposure and Risks**

The submitted nontarget plant studies, waiver requests, and accompanying justifications, fulfill the respective EPA requirements for the ecological risk assessment of a microbial pesticide. No adverse effects to nontarget populations of avian, freshwater fish, aquatic invertebrates, plants or their respective endangered taxa are expected to result from the intended pesticidal use of *ZYMV-WK*.

Nontarget toxicity tests were waived for wild mammal, avian oral toxicity/pathogenicity, avian injection toxicity/pathogenicity, freshwater aquatic invertebrate, estuarine and marine animal, and nontarget insect, and honeybees [Section III.C.1.f.].

In the unlikely event that nontarget organisms are affected during the commercial application of this product, such incidents should immediately be reported to the EPA, as required under FIFRA Section 6(a)(2), so that the Agency may take appropriate action.

### **Data Gaps and Requirements/Labeling**

There are no data deficiencies for *ZYMV-WK*. 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

<b>Biological Name:</b>	<i>Zucchini Yellow Mosaic Virus - Weak Strain</i>
<b>ATCC Number:</b>	ATCC PV-593
<b>Trade/Other Names:</b>	AgroGuard™, Curbit™
<b>OPP Chemical Code:</b>	244201
<b>Basic Manufacturer:</b>	Bio-Oz Biotechnologies, Ltd.

### B. Use Profile

<b>Type of Pesticide:</b>	Microbial pesticide, plant viruscide
<b>Use Sites:</b>	Young plants in the Cucurbitaceae family (squash, watermelon, melons, cucumbers) before transplanting in the field
<b>Target Pests:</b>	Protect plants against severe infections by Zucchini Yellow Mosaic Virus
<b>Formulation Types:</b>	Liquid
<b>Method/Rate of Application:</b>	In greenhouse or other environments, under positive pressures, the pesticide is directly sprayed on young cucurbit seedlings at the rate of ca. 0.05 mg ZYMV-WK virions/L of product.

### C. Estimated Usage

An estimate of usage, based on the existing commercial use patterns of similar products, cannot be made since these are the first U.S. pesticide registrations containing *ZYMV-WK* as the active ingredient.

### D. Data Requirements

Data and accompanying information, submitted under section 3(c)(5) of FIFRA in support of this unconditional registration, have been reviewed by the EPA. Product identity and analysis data, as well as documents submitted for acute mammalian toxicity and ecological effects, meet the requirements set forth for the proposed use patterns. If label instructions are followed, the Agency foresees no unreasonable adverse affects to human health and the environment from use of *Zucchini Yellow Mosaic Virus - Weak Strain*.

### E. Regulatory History

#### 1. Experimental Use and Temporary Tolerance Exemption

No EUPs or temporary tolerance exemptions have been issued for *Zucchini Yellow Mosaic Virus - Weak Strain*.

## **2. Section 3 Registration and Exemption from Tolerance**

On February 28, 2006, the USDA-IR4, on behalf of Bio-Oz Advanced Biotechnological Agricultural, Inc. submitted an application to EPA to register the active ingredient, *ZYMV-WK* as a microbial pesticide. When the application package for the new active ingredient was deemed complete, receipt of the application was published in the Federal Register [FR: June 9, 2006, Vol. 71, No 111, pp. 33446-33448]. The Agency received no comments on the FR announcement.

Concomitant with the application for the Section 3(c) registration, the registrant filed a petition (PP 6E7050) requesting a permanent exemption from the requirement of a tolerance for the active ingredient, *ZYMV-WK* on cucurbit commodities. A notice of filing of this petition was published in the Federal Register [FR: June 14, 2006, Vol. 71, No. 114, pp.34338-34340]. An exemption from the requirement of a tolerance for residues of *ZYMV-WK* on cucurbit commodities is being processed in connection with this petition and the final rule will be published in the Federal Register (40 CFR Part 180), concurrent with the unconditional registration.

### III. RISK ASSESSMENT

#### A. Physical and Chemical Properties Assessment

The data submitted in support of product identity requirements for *Zucchini Yellow Mosaic Virus - Weak Strain* (hereafter referred to as *ZYMV-WK*) are sufficient for the proposed use patterns of the microbial pesticide (Table 1).

**Table 1: Product identity and manufacturing process data requirements for *ZYMV-WK*.**

Test Guideline	Data Requirement	MRID	Study Classification	Data Requirement Status <sup>c</sup>
151-20 <sup>a</sup> 885.1100 <sup>b</sup>	Product identity	467854-01; 467854-02	ACCEPTABLE	FULFILLED
151-21 885.1200	Manufacturing process	467854-03	ACCEPTABLE	FULFILLED
151-22 885.1300	Discussion of formation of unintentional ingredients	467854-03	ACCEPTABLE	FULFILLED
151-23 885.1400	Analysis of samples	467854-04	ACCEPTABLE	FULFILLED
151-25 885.1500	Certification of limits	467854-05	ACCEPTABLE	FULFILLED
151-25 830.1800	Enforcement analytical method	467854-03	ACCEPTABLE	FULFILLED
151-26	Physical and chemical properties	Self-Certification Form 8570-36; 467854-03	ACCEPTABLE	FULFILLED

<sup>a</sup>Microbial Pesticide Guidelines Reference No. (40 CFR 158.740)

<sup>b</sup>OPPTS Microbial Pesticide Test Guidelines

<sup>c</sup>Fulfilled = Data Requirement Complete

#### **1. Product Identity and Mode of Action (MRIDs 46785401 and 46785402; Gdln . 151-26; OPPTS Guidelines 885.1100, 885.1200, 885.1300, 885.1400, 885.1500; 830.1800)**

AgroGuard™ Z is an end use product and manufacturing use product, having the same formulation and containing the same amount of *ZYMV-WK* as the active ingredient at 0.05 mg virions/L. *ZYMV-WK* is a positive, single-stranded RNA plant virus and is taxonomically classified as a member of the Potyviridae. It was originally isolated from a melon branch which showed weak symptoms of the

severe disease, Zucchini Yellow Mosaic Virus. It has flexuous filaments (~ 750 nm length) and forms plant aggregates, e.g., cytoplasmic pinwheels and scrolls, as well as fibrillar material.

*Zucchini Yellow Mosaic Virus - Weak Strain* is a natural plant virus isolate and replicates only in susceptible plant hosts. This weak strain of ZYMV does not cause overt plant disease and appears to stimulate plant viral defenses against severe strains of ZYMV. It does not replicate in aphids and is poorly-transmitted by these insect vectors.

ZYMV-WK is commercially available as Curbit™ in the EU, Israel and in the UK. A variant of this pesticide has also been reportedly used in Hawaii.

There are no impurities of toxicological significance associated with ZYMV-WK; and the inert ingredients are not known to be toxic, irritating or allergenic. Pathogens to humans or animals are not expected due to sterile manufacturing processes (BPPD Reviews dated January 31, 2007).

**2. Physical and Chemical Properties Assessment (MRIDs 46785401, 46785402, 46785403; OPPTS 830.6302, 830.6303, 830.7000, 830.7300, 830.6320, 830.6317; Table 1. OPP Gdln. 151-26)**

The end use product (same as the manufacturing use product) is a dark green liquid at 4° C and a pH of 6.1 (range = 5.9-6.3) with a bulk density of 8.3 lbs/gallon. It is reportedly stable for 14 days at 4° C. Other Physical and Chemical Properties are provided in Table 2. (BPPD Review –January 31, 2007).

<b>Guideline No./Property</b>	<b>Description of Result</b>	<b>Methods</b>
830.6302 Color	Dark green liquid	467854-03
830.6303 Physical State	EP is a Fluid.	467854-03
830.6304 Odor	Aroma of crushed squash leaves	467854-03
830.6313 Stability	Not applicable; Product is not chemically reactive.	467854-02; 467854-03
830.6314 Oxidation/Reduction	Not applicable; Product does not contain oxidizing or reducing agents.	467854-02; 467854-03
830.6315 Flammability	Not applicable; Product does not contain combustible liquids.	467854-02; 467854-03
830.6316 Explodability	Not applicable; Product does not contain potentially explosive components.	467854-02; 467854-03
830.6317 Storage Stability	Stable at 4°C for 14 days	467854-03
830.6319 Miscibility	Not applicable; Product is not emulsifiable or diluted with petroleum solvents.	467854-02; 467854-03
830.6320 Corrosion Characteristics	Not applicable; Product is not chemically reactive.	467854-02; 467854-03
830.6321 Dielectric Breakdown Voltage	Not applicable; Product is not intended for use around electrical equipment.	Label
830.7000 pH	6.1 ± 0.2	467854-03
830.7100 Viscosity	Similar to water.	467854-03
830.7200 Melting Range	Not applicable; Product is not a solid.	467854-02; 467854-03
830.7220 Boiling Range	Not applicable; TGAI is a solid.	467854-02; 467854-03
830.7300 Bulk Density	8.3 lbs./gal.	467854-02
830.7370 Dissociation Constant in Water	Not applicable; TGAI is not ionic.	467854-02; 467854-03
830.7550/60/70 Partition Coefficients	Not applicable; Product is not organic or non-polar.	467854-02; 467854-03
830.7840/60 Water Solubility	Settling may occur – shake mixtures prior to use.	Label
830.7950 Vapor Pressure	Not applicable; TGAI is a biological entity and should not evaporate.	467854-02

## **B. Human Health Assessment**

The submitted mammalian toxicology waiver requests and rationale are sufficient to support the unconditional registration of ZYMV-WK for the proposed use patterns.

### **1. Toxicological Hazard Assessment**

Summaries of submitted toxicology waiver requests with accompanying rationale (Table 3) are discussed below.

**Table 3. Tier I – Microbial pesticides toxicology data requirements for Zucchini Yellow Mosaic Virus - Weak Strain.**

Test Guideline	Data Requirement	Toxicity Category	MRID #	Study Classification	Data Requirement Status <sup>c</sup>
152-30 <sup>a</sup> 885.3050 <sup>b</sup>	Acute oral toxicity	III	467854-17 467854-19 470083-01	ACCEPTABLE WAIVER RATIONALE; Routine exposures to naturally-occurring plant viruses have not led to any known adverse effects to mammalian health; plant viruses do not infect mammalian cells, nor replicate in mammals	FULFILLED
152-31 885.3100	Acute dermal toxicity	III	467854-17 467854-19 470083-01	ACCEPTABLE WAIVER RATIONALE	FULFILLED
152-32 885.3150	Acute pulmonary toxicity/ pathogenicity	III	467854-17 467854-19 470083-01	ACCEPTABLE WAIVER RATIONALE	FULFILLED
152-33 885.3200	Acute injection toxicity/pathogenicity	III	467854-17 467854-19 470083-01	ACCEPTABLE WAIVER RATIONALE	FULFILLED
152-34 870.2500	Primary dermal irritation	III	467854-17 467854-19 470083-01	ACCEPTABLE WAIVER RATIONALE	FULFILLED
152-35 870.2400	Primary eye irritation	III	467854-17 467854-19 470083-01	ACCEPTABLE WAIVER RATIONALE	FULFILLED
152-16A 885.3500	Cell Culture	-	467854-17 467854-19 470083-01	ACCEPTABLE WAIVER RATIONALE	FULFILLED
152A-20 885.3550	Acute Toxicology Tier 2	-	467854-19	Supplemental –Study not required	Not required
152A-21 885.3600	Subchronic Toxicity and Pathogenicity	-	467854-19	Supplemental–Study not required	Not required
152A-30 885.3650	Reproductive and Fertility Effects	-	467854-19	Supplemental–Study not required	Not required
152-38	Immune Response		467854-17	ACCEPTABLE WAIVER RATIONALE	FULFILLED

<sup>a</sup>Microbial Pesticide Guidelines Reference No. (40 CFR 158.740)

<sup>b</sup>OPPTS Microbial Pesticide Test Guidelines.

<sup>c</sup>Fulfilled = Data Requirement Complete

- a. Acute Oral Toxicity –Waiver Request Granted (Gdln. 152-30; OPPTS Gdln. 885.3050)**
- b. Acute Dermal Toxicity Data –Waiver Request Granted (Gdln. 152-31; OPPTS Gdln. 870.1200)**
- c. Acute Inhalation Toxicity –Waiver Request Granted (Gdln. 152-32; OPPTS Gdln. 870.1300)**
- d. Acute Pulmonary Toxicity/Pathogenicity–Waiver Request Granted (Gdln. 152-32; OPPTS Gdln. 885.3150)**
- e. Acute Injection Toxicity/Pathogenicity–Waiver Request Granted (Gdln. 152-33; OPPTS Gdln. 885.3200)**
- f. Primary Dermal Irritation–Waiver Request Granted (Gdln. 152-34; OPPTS Gdln.870.2500)**
- g. Acute Eye Irritation–Waiver Request Granted (Gdln. 152-35; OPPTS Gdln.870.2400)**
- h. Immune Response-Waiver Request Granted (Gdln. 152-38)**

(MRIDs 467854-17; 467854-19; 470083-01)

***Waiver Rationale:***

**a.-h.** Several factors were taken into consideration for waiving the above data requirements for acute mammalian health effects following exposure(s) to *Zucchini Yellow Mosaic Virus - Weak Strain*. Routine exposure of farm personnel, consumers and laboratory researchers has occurred for naturally-occurring plant viruses, such as ZYMV and similar plant viruses (e.g., potyviruses; and Tomato Mosaic Virus – ToMV – a tobamovirus). This has not led to any known adverse effects; there are “[n]o reports of ill-health, sensitization or allergenicity” from these plant viruses to humans or other vertebrates, even after the use of *ZYMV-WK* as a pesticide in the EU, Israel and Hawaii. Plant viruses are not known to infect mammalian cells and replicate in mammals, however some plant viruses may replicate in eukaryotic vectors, such as persistent viruses in aphids. *ZYMV-WK* is vectored in a non-persistent manner; that is, it does not replicate in insect hosts. Since plant viruses are not known to produce toxic compounds or directly damage tissues – and cannot directly infect plant cells (a vector is needed to provide mechanical infection to plants) — it is “highly unlikely” that the intended uses of *ZYMV-WK* would result in any harm to mammalian organisms. No health effects were noticed when several similar infectious plant viruses (including *ZYMV-WK*) were repeatedly injected into rabbits to detect polyclonal antibody production over several weeks (MRID 467854-17), based on 1986-1996 lab records. Application of *ZYMV-WK* to plants as a pesticide occurs inside an applicator machine in a semi-contained environment, leading to a very low potential for worker exposure to the concentrated pesticide.

**i. Cell Culture –Waiver Request Granted (MRID 467854-17, 467854-19; Gdln. 152A-16; OPPTS Gdln. 885.3300)**

These tests are designed to provide information on the ability of viral pest control agents to infect, replicate in, transform or cause toxicity in, mammalian cell lines. Plant viruses are not known to infect mammalian cells and replicate in mammals; plant viruses are not known to produce toxic compounds or directly damage tissues and directly infect plant cells (a vector is required for mechanical infection to plants). Furthermore, no health effects were noticed when several similar infectious plant viruses (including *ZYMV-WK*) were repeatedly injected into rabbits to detect polyclonal antibody production over several weeks, in studies conducted in a 10-year period, according to 1986-1996 lab records.

**j. Acute Toxicology Tier 2 - Supplemental-Not required (MRID 467854-17; Gdln. 152A-20; OPPTS Gdln. 885.3550)**

Based on the data generated in accordance with Tier I data requirements (40 CFR Part §158.740(c)), Tier II tests (Guidelines 152B-40 through 152B-49), which include acute oral, acute inhalation, acute intraperitoneal/intracerebral, primary dermal, primary eye, immune response, teratogenicity, virulence enhancement, and mammalian mutagenicity, were not required.

**k. Subchronic Toxicity and Pathogenicity – Supplemental-Not required (MRID 467854-17; Gdln. 152A-21; OPPTS Gdln. 885.3600)**

Based on the data generated in accordance with Tier I data requirements (40 CFR Part §158.740(c)), Tier II subchronic toxicity and pathogenicity tests were not required.

**l. Subchronic, Chronic Toxicity and Oncogenicity**

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

**m. Effects on the Endocrine System**

EPA is required under section 408(p) of 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." *Zucchini Yellow Mosaic Virus – Weak Strain* is not a known endocrine disruptor nor is it related to any class of known endocrine disruptors.

Consequently, endocrine-related concerns did not adversely impact the Agency's safety finding for *Zucchini Yellow Mosaic Virus - Weak Strain*.



## 2. Dietary Exposure Assessment

### a. Food Clearances/Tolerances

This is the first proposed Section 3(c)(5) unconditional registration of *ZYMV-WK*. There is zero to negligible potential for toxicity, and justifiable waiver requests and rationale adequately support a determination of a lack of adverse effects through oral, inhalation, dermal, and eye routes of exposure. The ecology of naturally occurring strains of *ZYMV* and other plant viruses is such that routine exposure among farm and laboratory personnel, and consumers has occurred for a long history of these plant viruses, which have not led to any known adverse effects. Therefore, the Agency has determined that there is a reasonable certainty that no harm is likely to result from exposure to the active ingredient. 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 *ZYMV-WK* is being established concomitant with the unconditional registration (40 CFR Part 180).

### b. Dietary Risk Characterization

The mode of action for *ZYMV-WK* to protect Cucurbitaceae against severe *ZYMV* involves intentionally inoculating healthy plants to prevent infection by more virulent *ZYMV* strains. Plant viruses are not known to infect mammalian cells and replicate in mammals. Virus-infected food plants have always been in the human and domestic animal food supply. Most plants may be infected by at least one virus, and components of plant viruses are often present in the produce of crop plants. Zucchini Yellow Mosaic Virus is not new to the U.S., nor to the food supply; the first reports of *ZYMV* in the United States were in 1981. To date, there have been no reports of adverse human or animal health effects associated with consumption of plant viruses in food. Therefore, EPA concludes that intended uses of *ZYMV-WK* on cucurbit plants pose negligible to no risk for the general population, including infants and children (BPPD Reviews – January 31, 2007 and March 22, 2007).

### c. Drinking Water Risk Characterization

*ZYMV-WK* is not intended for use in drinking water or other aquatic bodies; nor are its uses likely to result in this virus reaching surface water or ground water that might be used as potable water. In the unlikely event that *ZYMV-WK* would reach water consumed by humans, the Agency concludes that there is reasonable certainty that no harm will result to humans from all anticipated exposures through water to any residues resulting from these intended uses, due to the lack of infectivity of plant viruses in humans.

### d. Acute and Chronic Dietary Risks for Sensitive Subpopulations Particularly 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 *ZYMV-WK* as a microbial pest control agent. This includes all anticipated dietary exposures and all other exposures for which there is reliable information. *ZYMV-WK* is a weak strain of Zucchini Yellow Mosaic Virus of cucurbit plants; and

*ZYMV-WK* is not toxic, not pathogenic and not infective to mammals. Therefore, exempting *ZYMV-WK* from the requirement of a tolerance is considered safe and poses no significant risks.

**e. 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 *ZYMV-WK* 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 Section III.B.2 above, *ZYMV-WK* is non-toxic, non-pathogenic, and non-infective to mammals. Accordingly, exempting *ZYMV-WK* from the requirement of a tolerance is considered safe and poses 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), which often are referred to as uncertainty factors, 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. As mentioned previously in the toxicological profile, humans, including infants and children, are commonly exposed to plant viruses through food, where they are commonly found, with no known or reported adverse effects. As discussed previously, the Agency has concluded that *ZYMV-WK* is non-toxic to mammals, including infants and children. Because there are no threshold levels of concern to infants, children, and adults when *ZYMV-WK* is used as labeled, the Agency has determined that an additional margin of safety for infants and children is unnecessary.

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

The potential for aggregate exposure should be adequately mitigated if label instructions are followed.

**i. Dermal**

Dermal exposure is limited by use of the required PPE in occupational settings, and workers are advised to avoid skin contact and to wash any exposed skin or clothing (see Section III.B.4).

**ii. Oral**

Oral exposure would occur primarily from eating treated produce, specifically cucurbits. However, negligible to no risk is expected, because *ZYMV-WK* is a plant virus and as such, is non-toxic, non-pathogenic and non-infective to animals, including humans. Based on the acute oral toxicity study, the pesticide is classified as Toxicity Category IV for oral exposure (BPPD Review—January 31, 2007; for more discussion, see Section III.B.3).

### **iii. Inhalation**

The greatest likelihood of inhalation exposure would occur in an occupational setting, among mixers/loaders and applicators. However, as summarized in the above text, *ZYMV-WK* is a weak plant virus and is non-infective, non-pathogenic, and non-toxic to mammals, including humans. Despite the benign nature of the active ingredient, the Agency requires that all workers exposed to microbial pesticides wear a dust/mist filtering respirator. As such, the risks anticipated for inhalation exposure are considered minimal.

### **g. Cumulative Effects**

Section 408(b)(2)(D)(v) of the FFDCFA requires the Agency to consider the cumulative effect of exposure to *ZYMV-WK* 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. As determined in Section III.B.2 above, *ZYMV-WK* is non-toxic and non-pathogenic to mammals. Consequently, no cumulative effects from the residues of this product with other related microbial pesticides are anticipated.

## **3. Occupational and Residential Risk Characterization**

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

Zucchini Yellow Mosaic Virus - Weak Strain will be applied to young cucurbit plants in a semi-contained environment before transplanting to an agricultural field for further crop and fruit development. Although some applications may be made near residential areas, no harm would be expected to result from exposure to *ZYMV-WK* due to its low toxicity classification (see Section III.B.2 above) and due to the directed method of application in semi-contained environments.

### **b. Occupational Exposure and Risk**

Potential worker and pesticide handler exposure to *ZYMV-WK* is not expected to pose any undue risk. Appropriate Personal Protective Equipment (PPE) 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. To perform post-application activities, early entry workers must wear coveralls in addition to the PPE described above.

The primary routes of exposure for mixer/loaders and applicators would be dermal and/or inhalation exposure. The waiver requests and accompanying justification for the acute toxicity/pathogenicity studies and additional OPPTS requirements (see Table 2) submitted in support of the registration demonstrated that *ZYMV-WK* is non-toxic, non-pathogenic and non-infective to mammalian organisms. As such, the risks anticipated for occupational exposure are considered minimal (Section III.B.2 above).

## C. Environmental Assessment

### 1. Ecological Effects Hazard Assessment

Below is a summary of the ecological effects database evaluated in support of this action (Table 4). A determination of reasonable certainty that no incremental irreversible adverse effects to wild mammals, avian species, insects including beneficial insects, freshwater fish, aquatic invertebrates, estuarine and marine animals or to the vast majority of plant species will result from the intended applications to cucurbit crops. The database consists of acceptable waiver requests supported by scientific rationale and submitted data that support the conclusion that there are no incremental irreversible hazards to nontarget organisms as a result of intended uses of *ZYMV-WK*.

**Table 4. Tier I – Microbial pesticides nontarget organism data requirements for *ZYMV-WK*.**

Test Guideline	Data Requirement	MRID Nos.	Study Classification	Data Requirement Status <sup>c</sup>
154-16 <sup>a</sup> 885.4050 <sup>b</sup>	Avian oral	46785408 46785423	ACCEPTABLE WAIVER RATIONALE	FULFILLED
154-17 885.4100	Avian injection	46785423	ACCEPTABLE WAIVER RATIONALE	FULFILLED
154-18 885.4150	Wild mammal	46785423	ACCEPTABLE WAIVER RATIONALE	FULFILLED
154-19 885.4200	Freshwater fish	46785423	ACCEPTABLE WAIVER RATIONALE	FULFILLED
154-20 885.4240	Freshwater aquatic invertebrate	46785423	ACCEPTABLE WAIVER RATIONALE	FULFILLED
154-21 885.4280	Estuarine and marine animal	46785423	ACCEPTABLE WAIVER RATIONALE	FULFILLED
154-22 885.4300	Nontarget plant	46785408 46785421 46785422 47008302	ACCEPTABLE WAIVER RATIONALE. The majority of the submitted published literature and 2 independent studies document that the MPCA, <i>ZYMV-WK</i> differs from other <i>ZYMV</i> strains (i.e., those that cause severe disease) in terms of plant host range and transmission potential, and that natural infections are predominantly restricted to the Cucurbit family. In experimental settings, latent, localized, non-systemic <i>ZYMV-WK</i> infections have been noted following artificial inoculation in several tested plant species.	FULFILLED

			Unlike ZYMV, ZYMV-WK is poorly aphid-transmitted. In a study designed to investigate potential synergism of ZYMV-WK with other cucurbit plant viruses, there was no increase in the severity of symptoms in plants challenged with cucurbit viruses + ZYMV-WK compared with those plants challenged with only ZYMV-WK. For complete text, refer to Item <b>III.C.1.g. Nontarget Plants</b>	
154-23* 885.4340**	Nontarget insect testing	46785423	ACCEPTABLE WAIVER RATIONALE	FULFILLED
154-24 885.4380	Honey bee testing	46785423	ACCEPTABLE WAIVER RATIONALE	FULFILLED
155A-1,2 885.5000	Background for microbial Pesticides testing	46785424	ACCEPTABLE WAIVER RATIONALE	FULFILLED
155A-10 885.5200	Expression in a terrestrial Environment	46785425	ACCEPTABLE WAIVER RATIONALE	FULFILLED
155A-11 885.5300	Expression in a freshwater Environment	46785425	ACCEPTABLE WAIVER RATIONALE	FULFILLED
155A-12 885.5400	Expression in a marine or estuarine environment	46785425	ACCEPTABLE WAIVER RATIONALE	FULFILLED

<sup>a</sup>Microbial Pesticide Guidelines Reference No. (40CFR 158.740)

<sup>b</sup>OPPTS Microbial Pesticide Test Guidelines

<sup>c</sup>Fulfilled = Data Requirement Complete

- a. Avian Oral- Waiver Request Granted (MRID 46785423; Gdln. 154-16; OPPTS Gdln. 885.4050)**
- b. Avian Injection- Waiver Request Granted (MRID 46785423; Gdln. 154-17; OPPTS Gdln. 885.4100)**
- c. Wild Mammal- Waiver Request Granted (MRID 46785423; Gdln. 154-18; OPPTS Gdln. 885.4150)**
- d. Freshwater Fish Waiver Request Granted (MRID 46785423; Gdln. 154-19; OPPTS Gdln. 885.4200)**
- e. Freshwater Aquatic Invertebrate- Waiver Request Granted (MRID 46785423; Gdln. 154-20; OPPTS Gdln. 885.4240)**

**f. Estuarine/Marine Organisms- Waiver Request Granted (MRID 46785423; Gdln. 154-21; OPPTS Gdln. 885.4280)**

(MRIDs 46785408 and 46785423)

**Waiver Rationale:**

**a.-f.** Zucchini Yellow Mosaic Virus - Weak Strain is a naturally occurring strain of zucchini yellow mosaic virus (ZYMV) and was originally isolated in France in 1986 by H. Lecoq (Lecoq, H. et.al., 1991). ZYMV is a plant virus and there is no evidence that plant viruses are capable of infecting animal hosts. In addition, there are no known toxins or metabolites produced by severe strains of ZYMV or by ZYMV-WK that could cause harm to animals or the environment. Although ZYMV-WK has a high level of sequence identity to severe strains of ZYMV, the symptoms of its infection are not as debilitating or destructive, and it does not cause losses in yield. The levels of the ZYMV-WK in artificially-inoculated plants are no higher than those attained in plants naturally inoculated with severe ZYMV; early treatment with the weak strain will substitute for the presence of severe ZYMV. Currently, ZYMV is endemic to cucurbit crops (BPPD Review – March 22, 2007).

**g. Nontarget Plant (MRIDs 46785408, 46785421, 46785422, 47008302;Gdln 154-22; OPPTS Gdln. 885.4300)**

To satisfy this requirement, the registrant provided documentation and experimental evidence regarding the differences in host range and transmission potential of *ZYMV-WK* when compared with the more severe ZYMV. The majority of the published literature and 2 independent studies document that the MPCA, *ZYMV-WK* differs from wild-type severe ZYMV in terms of plant host range and transmission potential, and that natural infections are probably restricted to the Cucurbit family. The experimental host range of ZYMV includes members of 11 families of dicotyledons. Most plants outside the Cucurbitaceae that were infected with ZYMV in experimental settings resulted in latent infections, and/or localized lesions (restricted to the site of infection) and other non-systemic effects while testing positive for infection. Natural infection by ZYMV has been reported mostly in the family Cucurbitaceae. (BPPD Review – March 22, 2007).

*ZYMV-WK* is poorly aphid-transmitted when compared to severe strains of ZYMV; furthermore it has never been reported that *ZYMV-WK* can be transmitted alone by aphids. The lack of persistence and replication in aphids is apparently due to two natural mutations in a helper component gene in *ZYMV-WK*, unlike other ZYMV strains that may cause severe cucurbit disease and are transmitted by aphids. Under experimental conditions helper components of other cucurbit potyviruses (e.g., watermelon mosaic virus - WMV) can assist in the transmission of ZYMV. (BPPD review – January 31, 2007).

The registrant also submitted a study which provided experimental evidence that there was little to no probability of synergistic interaction between *ZYMV-WK* and other cucurbit viruses. Under controlled conditions, squash plantlets were artificially-inoculated with *ZYMV-WK* using the standard procedure

developed by the registrant and the *ZYMV-WK*- treated plants were transplanted into a “semi-contained structure” and protected with a nylon cover five days after inoculation. Fourteen days after inoculation plants were confirmed by ELISA for infection with *ZYMV-WK*; uninfected plants were excluded from the experiment. Remaining plants were challenged with additional virus(-es), or remained unchallenged, for a total of 12 treatments: (1) healthy, untreated control; (2) *ZYMV-WK* only; (3) *ZYMV-WK* with *ZYMV-JV* (Jordan Valley, local virulent strain); (4) *ZYMV-JV* only; (5) Cucumber Vein Yellow Virus (CVYV) only; (6) CVYV with *ZYMV-WK*; (7) Papaya Ring Spot Virus (PRSV) only; (8) PRSV with *ZYMV-WK*; (9) Watermelon Mosaic Virus II (WMV II) only; (10) WMV II and *ZYMV-WK*; (11) Cucumber Mosaic Virus (CMV) only; and (12) CMV and *ZYMV-WK*. All plants were confirmed by ELISA to be infected with the appropriate challenge virus two weeks after the plants were challenged. For the remainder of the experiment fruit was collected every 3 to 4 days until the end of the experiment (63 days) and classified as marketable or non-marketable. There were no reductions in fruit yield nor fruit quality from plants treated only with *ZYMV-WK* compared to healthy control plants. Significant reductions in fruit yield were noted in unprotected plants that were challenged with *ZYMV-JV* (severe strain). There was no increase in the severity of symptoms in plants infected with *ZYMV-WK* and challenged with other cucurbit viruses (PRSV, WMV, CMV, and CVYV) Therefore, it is anticipated that protected plants with *ZYMV-WK* and subsequently infected by secondary cucurbit viruses (including severe *ZYMV*) in a field situation will likely not result in amplified symptomatology nor disease.

**h. Nontarget Insects- Waiver Request Granted (MRID 46785423; Gdln. 154-23; OPPTS Gdln. 885.4340)**

See section III.C.1.a-f above for waiver justification. *ZYMV* and *ZYMV-WK* do not replicate in aphids, although some plant viruses may replicate in aphids without symptom or adverse effects to this insect pest.

**i. Honeybees- Waiver Request Granted (MRID 46785423; Gdln. 154-24; OPPTS 885.4380)**

See section III.C.1.a-f above for waiver justification.

**j. Expression in a Terrestrial Environment- Waiver Request Granted (MRID 46785425; Gdln. 155A-10; OPPTS 885.5200)**

The active ingredient, *Zucchini Yellow Mosaic Virus - Weak Strain (ZYMV-WK)* is a naturally occurring strain of zucchini yellow mosaic (*ZYMV*) and the intended uses in semi-contained environments are not expected to result in increased exposure or adverse effects to humans or animals. Also as plant viruses, *ZYMV* (severe and *ZYMV-WK*) cannot persist outside host plants, and therefore cannot multiply outside the susceptible plant families. *ZYMV* is aphid transmitted; the mild strain of *ZYMV* is poorly transmitted and therefore the risk of mobility via this route is significantly lower than that of severe naturally occurring strains of the same virus (*ZYMV*). Additional rationale is included in section III.C.1.a.

**k. Expression in a Freshwater Environment - Waiver Request Granted (MRID 46785425; Gdln. 155A-11; OPPTS 885.5300)**

See section III.C.1.j above for waiver justification.

**l. Expression in a Marine/Estuarine Environment - - Waiver Request Granted (MRID 46785425; Gdln. 155A-12; OPPTS 885.5400)**

See section III.C.1.j above for waiver justification.

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

*Zucchini Yellow Mosaic Virus - Weak Strain (ZYMV-WK)* is a naturally occurring, weakly virulent strain of zucchini yellow mosaic (ZYMV); ZYMV is endemic to domestic plantings of cucurbit crops, such as zucchini, watermelon and cantaloupe. The original strain *ZYMV-WK* (ATCC Acc. # PV-593) was isolated from infected melon plants in France in 1986; and ZYMV was first reported in 1981 in the U.S. Although the experimental host range of ZYMV includes members of 11 families of dicotyledons; severe disease symptoms, including yield reductions are predominantly restricted to members of the Cucurbit family. Most plants outside the Cucurbitaceae that were infected with ZYMV in experimental settings resulted in latent infections, and/or localized lesions (restricted to the site of infection) and other non-systemic effects.

Unlike severe ZYMV strains, *ZYMV-WK* is poorly aphid transmitted, and it has never been reported that *ZYMV-WK* can be transmitted alone by aphids. *ZYMV-WK* replicates only in susceptible plant hosts and is not known to cause overt plant disease. This ability to replicate but not cause disease makes this isolate useful for 'cross-protection' against disease-causing strains of ZYMV, by allowing the plant to initiate a defense reaction, commonly referred to as post transcriptional gene silencing.

The cross-protection phenomenon of *ZYMV-WK* involves "the use of a mild strain of a virus to protect against the economic damage by severe strains of the same virus". In this phenomenon, plants that are already infected with a virus are normally protected against infection by a related strain of the virus. Successful implementation of cross-protection by *ZYMV-WK* has been notably demonstrated in Taiwan, several European countries, the U.K. and in Israel. The usefulness of cross protection using *ZYMV-WK* was also demonstrated recently with cantaloupe plants tested in field enclosures in California. Cross protected plants conserved marketable fruit yield by nearly 75% upon subsequent infection with a severe ZYMV strain. (Fuchs, et al., 1997).

The ecological data (as summarized in section III.C.1 above) support a conclusion that no incremental irreversible hazards to nontarget organisms or to the environment are expected as a result of intended uses of *ZYMV-WK* (AgroGuard Z™). These data and information support labeled terrestrial uses on cucurbit crops within semi-contained environments, before transplanting to a commercial field. Accordingly, OPPTS Tier I testing for ecological effects or environmental expression is not required. In the unlikely event that some nontarget organisms are affected during the commercial application of



this product, such incidents should be immediately reported to the EPA as required under FIFRA Section 6(a)(2) so that the Agency may take appropriate action.

### **3. Endangered Species Assessment**

The intended uses of this product, once per crop season under semi-contained conditions provides EPA with confidence that plants inoculated with *ZYMV-WK* will not pose a risk to threatened and endangered species (including plants). *ZYMV* is the targeted plant virus and there is no evidence that plant viruses are capable of infecting animal hosts and posing a risk to threatened or endangered animal species. The MPCA, *ZYMV-WK* is a naturally-occurring mild strain of *ZYMV* whose level in the environment will not significantly increase when inoculated plants are planted in the field (BPPD Review – March 22, 2007).

Studies using *ZYMV-WK* and plants that are susceptible to *ZYMV* resulted in no negative effects (MRIDs 467854-22 and 470083-02). Therefore, it is unlikely that nontarget plants would be adversely affected if *ZYMV-WK* was somehow transmitted. It has never been reported that *ZYMV-WK* can be transmitted naturally by aphids in the field. In laboratory studies it has been shown that the helper-components of some other cucurbit viruses can aid in the transmission of *ZYMV* but this has not been confirmed in a field setting. Therefore, it is unlikely that other plants, even those susceptible to more virulent strains of *ZYMV*, will become infected with *ZYMV-WK*.

Not all of the plants tested in experimental host range studies showed symptoms of *ZYMV* infection, but most tested positive for the virus using DAS-ELISA testing. EPA performed a search for threatened and endangered plant species belonging to the families tested in the submitted literature by using publicly available US Fish and Wildlife Service and NatureServe data ([www.fws.gov/endangered/wildlife.html](http://www.fws.gov/endangered/wildlife.html), [www.natureserve.org](http://www.natureserve.org)). Information about each species was gathered (for example, location of species, habitat preferences, and proximity to agriculture) for the threatened and endangered species belonging to those families. The threatened and endangered plant species that were in the families tested occur in areas where they would not be in close proximity to agriculture.

In conclusion, based on information submitted to the Agency and publicly available literature, growing plants inoculated with *ZYMV-WK* will not adversely affect threatened and endangered species, including plants. Therefore, no restrictions need to be placed on planting seedlings that have been inoculated with *ZYMV-WK*.

This analysis supports a “no effect” (NA) opinion to Federally listed Threatened and Endangered species from the intended applications as a viruscide to protect cucurbit crop plants from severe Zucchini Yellow Mosaic Virus.

Detailed rationale and justification are on file with the EPA as specified in the Memorandum: “Environmental Risk Assessment for Zucchini Yellow Mosaic Virus (*ZYMV-WK*) Used to Inoculate Cucurbit Seedlings.”

#### **D. Efficacy Data**

Efficacy data were not reviewed by the EPA because the products are intended for control of severe *ZYMV* disease on cucurbit crops, and will not be formulated into products for control of 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, *ZYMV-WK* 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 *ZYMV-WK* is not expected to cause unreasonable adverse effects when used according to label instructions. Therefore, *ZYMV-WK* is eligible for registration.

#### **B. Regulatory Position**

##### **1. Unconditional Registration**

The data requirements are fulfilled. Consequently, BPPD recommends unconditional registration of product(s) that contain *ZYMV-WK* as a new active ingredient (i.e., AgroGuardZ<sup>®</sup>).

##### **2. Tolerances for Food Uses and /or Exemptions**

EPA received a pesticide petition (PP 6E7050) from Bio-Oz Biotechnologies Ltd., Kibbutz Yad Mordechai, DN Hoff Ashkelon 79145, Israel, which proposed [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, *ZYMV-WK*, on young cucurbit crops.

EPA is issuing a notice establishing an exemption from the requirement of a tolerance for residues of *ZYMV-WK* in or on all cucurbit commodities (40 CFR Part 180).

### 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 Reregistrations

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 nontarget organisms (plants and wildlife), and to ground and surface water contamination through the proposed use of products containing *ZYMV-WK* 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.

## C. Use Sites

*Zucchini Yellow Mosaic Virus - Weak Strain* has been approved for the use sites listed in Table 5.

**Table 5: Approved use sites for *ZYMV-WK* pesticide product.**

End-use Product	Use Sites	Date of Registration
Agroguard™Z	Cucurbits (including cucumbers, cantaloupes, watermelons, muskmelons, winter and summer squash, pumpkins, zucchini, and other cucurbits)	August 6, 2007

## D. Labeling

The following information describes labeling and rationale for the approved end-use product.

It is EPA's position that the labeling for end-use products containing *ZYMV-WK* must comply with the pesticide labeling requirements in existence when such products are registered.

### 1. Human Health Hazards

#### a. 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 Part 156.10 and other applicable notices, such as, and including the WPS labeling. *Zucchini Yellow Mosaic Virus - Weak Strain* products with commercial use sites are not subject to the Worker Protection Standard; because the intended method of application involves direct injection of young cucurbit plants with a special inoculation apparatus. Precautionary statements and personal protective equipment (PPE) as specified below are in the User Safety Recommendations portion of the pesticide label.

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.

#### **b. Other Precautionary Labeling**

The Agency has examined the toxicological data base for *ZYMV-WK* and concluded that the precautionary labeling required (*i.e.* Signal Word, First Aid Statements, User Safety Recommendations 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 *ZYMV-WK* on a case-by-case basis.

### **2. Environmental Hazards**

The risk of nontarget organism/endangered species exposure to *ZYMV-WK* is minimal to nonexistent provided the following statements are placed in the environmental hazards statement:

“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.”

### **3. Application Rate**

It is the Agency's position that the labeling for the pesticide products containing *ZYMV-WK* must comply with the current pesticide labeling requirements.

#### **Agroguard™ Z:**

Before transplanting young cucurbit plants into field, apply 0.01 mm per plantlet using a BIM™ inoculation apparatus.

#### 4. Ingredient Statement

##### Agroguard™ Z:

Zucchini Yellow Mosaic Virus - Weak Strain*	0.000005 % (minimum 5x10 <sup>13</sup> virions/L)
Other Ingredients **	99.99 %
Total**	100.0 %

- \*mild strain of zucchini yellow mosaic virus
- \*\*extract of homogenized zucchini leaves

#### 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), OPP 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. BIBLIOGRAPHY

##### A. Studies Submitted in Support of this Registration

- 467854-01 Braverman, M. (2005) Overview of Microbial Pest Control Agent: AgroGuard Z. Received 23 March 2006.
- 467854-02 Braverman, M. (2005) Group A: Product Identity: AgroGuard Z. Received 23 March 2006.
- 467854-03 Braverman, M. (2005) Manufacturing Process: AgroGuard Z. Project Number: 0374B. Received 23 March 2006.
- 467854-04 Braverman, M. (2005) Group A: Discussion of Formation of Unintentional Ingredients: AgroGuard Z. Received 23 March 2006.
- 467854-05 Braverman, M. (2005) Group A: Certification of Limits: AgroGuard Z. Received 23 March 2006.
- 467854-06 Braverman, M. (2005) Group B: Background for Residue Analysis of MCPA: AgroGuard Z. Received 23 March 2006.

- 467854-07 Braverman, M. (2005) Group B: Background for Residue Analysis of MCPA. Received 23 March 2006.
- 467854-08 Braverman, M. (2005) Group B: Chemical Identity: AgroGuard Z. Received 23 March 2006.
- 467854-09 Braverman, M. (2005) Group B: Nature of the Residue in Plants: AgroGuard Z. Received 23 March 2006.
- 467854-10 Braverman, M. (2005) Group B: Nature of Residues in Animals: AgroGuard Z. Received 23 March 2006
- 467854-11 Braverman, M. (2005) Group B: Analytical Methods - Plants: AgroGuard Z. Received 23 March 2006.
- 467854-12 Braverman, M. (2005) Group B: Analytical Methods in Animals: AgroGuard Z. Received 23 March 2006.
- 467854-13 Braverman, M. (2005) Group B: Storage Stability: AgroGuard Z. Received 23 March 2006.
- 467854-14 Braverman, M. (2005) Group B: Magnitude of Residues in Plants: AgroGuard Z. Received 23 March 2006.
- 467854-15 Braverman, M. (2005) Group B: Magnitude of the Residues in Meat, Milk, Poultry, Eggs: AgroGuard Z. Received 23 March 2006.
- 467854-16 Braverman, M. (2005) Group B: Magnitude of the Residues in Water, Fish and Irrigated Crops: AgroGuard Z. Received 23 March 2006.
- 467854-17 Braverman, M. (2005) Group C: Background for Mammalian Toxicity, Pathogenicity and Infectivity: AgroGuard Z. Received 23 March 2006.
- 467854-19 Braverman, M. (2005) Group C: Acute Oral, Dermal, Pulmonary and Injection Toxicity/ Pathogenicity Cell Culture, Acute Toxicology Tier 2, Subchronic Toxicity/ Pathogenicity, Reproductive and Fertility Effects. Received 23 March 2006.
- 467854-20 Braverman, M. (2005) Group D: Background for Nontarget Organism Testing of Microbial Pest Control Agents. Received 23 March 2006.

- 467854-21 Braverman, M. (2005) Group D: Nontarget Plant Studies: AgroGuard Z. Received 23 March 2006.
- 467854-22 Braverman, M. (2005) Group D: Nontarget Plant Studies - Potential for Synergism: AgroGuard Z. Received 23 March 2006.
- 467854-23 Braverman, M. (2005) Group D: Avian Oral Tier 1, Avian Inhalation Test Tier 1, Wild Mammal Testing Tier 1, Freshwater Fish Testing Tier 1, Freshwater Aquatic Invertebrate Tier 1, Estuarine and Marine Animal Testing, Tier 1, Nontarget Insect Studies Tier 1, Honey Bee Testing Tier 1. Received 23 March 2006.
- 467854-24 Braverman, M. (2005) Group E: Environmental Expression: Background for Microbial Pesticides Testing: AgroGuard Z. Received 23 March 2006.
- 467854-25 Braverman, M. (2005) Group E: Expression in a Terrestrial Environment, Expression in a Freshwater Environment, Expression in a Marine or Estuarine Environment. Received 23 March 2006.
- 470083-01 Braverman, M. (2006) Waiver Request for Primary Eye Irritation: AgroGuard Z. Received 18 December 2006.
- 470083-03 Braverman, M. (2006) Non Guideline Study: Appendix 7 Tier II Summaries Microbial Pest Control Agent: Agro Guard Z. Received 18 December 2006.
- 470083-04 Braverman, M. (2006) Non-Guideline Study: Appendix 8 Tier II Summaries Microbial Pest Control Product: AgroGuard Z. Received 18 December 2006.

## **B. Federal Register Publications**

Federal Register: June 14, 2006 (Volume 71, Number 114) (Page 34338-34340). *Zucchini Yellow Mosaic Virus - Weak Strain*; Notice of Filing of Pesticide Petition for the Establishment of an Exemption from the Requirement of Regulations for Residues of Zucchini Yellow Mosaic Virus-Weak Strain (ZYMV-WK) in or on Cucurbits (PP 6E7050).

Federal Register: June 9, 2006 (Volume 71, Number 111 (Page 33446-33448)). *Zucchini Yellow Mosaic Virus - Weak Strain*; Pesticide Product; Registration Applications.

Registration of a New Active Ingredient (to be published in 2007).

Final Rule: Exemption from Tolerance (to be published in 2007).

### **C. BPPD Data Evaluation Records/Reviews**

Gagliardi, J. and Kough, J. (January 31, 2007). U.S. EPA/OPP/BPPD. AgroGuard™Z containing Zucchini Yellow Mosaic Virus – Weak Strain™ (ZYMV-WK)

Hunter, M. and Vaituzis, Z. (March 22, 2007). ). U.S. EPA/OPP/BPPD. Environmental Risk Assessment for Zucchini Yellow Mosaic Virus (ZYMV-WK) Used to Inoculate Cucurbit Seedlings. MRIDs 467854-08, 467854-20 through -25, 470083-02