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Draft Human Health and Ecological Risk Assessment for Lambda-cyhalothrin in Exotic Fruit Fly Applications

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Agency Contact:

John Stewart
National Fruit Fly Policy Manager
Plant Protection and Quarantine – Policy Management
Animal and Plant Health Inspection Service
U.S. Department of Agriculture
1730 Varsity Drive, Suite 400
Raleigh, NC 27606

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EXECUTIVE SUMMARY

United States Department of Agriculture (USDA), Animal and Plant Health Inspection Service (APHIS), Plant Protection and Quarantine (PPQ) is proposing to continue the use of the insecticide lambda-cyhalothrin in its cooperative exotic fruit fly eradication program. The formulation, Warrior II with Zeon Technology® (Warrior II), is a capsule suspension containing the active ingredient lambda-cyhalothrin (22.8%). The proposed application method is a soil application. The Warrior II formulation is a restricted use pesticide due to toxicity to fish and aquatic organisms. It is used only by certified applicators, or persons under their direct supervision, and only for those uses covered by the certified applicator's certification.

USDA-APHIS evaluated the potential human health and ecological risks from the proposed use of Warrior II in this assessment and determined that the risks to human health and the environment are negligible. Lambda-cyhalothrin has moderate acute oral, dermal, and inhalation toxicity in humans; however, the proposed method of application and adherence to label requirements substantially reduces the potential for exposure to humans and the environment, including nontarget fish and wildlife. Adverse health risk from accidental exposure such as splash to unprotected body areas is not expected for a well-trained certified applicator. Adverse health risk to the general public is not expected based on the soil drench application method and requirements for public notification, as well as destruction of fruit in treated areas as specified on the label. Adverse health risks from associated consumption of treated soil by children are also not expected based on conservative estimates of risk to this group of the population.

Off-site movement from lambda-cyhalothrin applications are expected to be minimized by the application method and environmental fate for the product. Risk to non-target terrestrial wildlife and invertebrates are expected to be minimal because of the targeted methods of application, where the product is applied, and the toxicity profile for lambda-cyhalothrin. Lambda-cyhalothrin is highly toxic to aquatic organisms; however, the method of application, environmental fate and current label restrictions regarding the protection of aquatic resources will minimize the risk.

1.0 INTRODUCTION

This human health and ecological risk assessment (HHERA) is a qualitative and quantitative evaluation of the potential risks and hazards to human health, non-target fish, and wildlife as a result of exposure to lambda-cyhalothrin under the proposed soil drench application to eradicate various species of exotic fruit flies (e.g., Mediterranean fruit fly, Mexican fruit fly, oriental fruit fly, etc.) that enter the United states.

The methods used to assess potential human health effects follow standard regulatory guidance and methodologies (NRC, 1983; USEPA, 2016), and generally conform to other Federal agencies such as the U.S. Environmental Protection Agency, Office of Pesticide Programs (USEPA/OPP). The methods used to assess potential ecological risk to non-target fish and wildlife follow USEPA and other published methodologies regarding eco-risk assessment.

The risk assessment is divided into four sections beginning with the problem formulation (identifying hazard), then a toxicity assessment (the dose-response assessment), and an exposure assessment (identifying potentially exposed populations and determining potential exposure pathways for these populations). In the fourth section (risk characterization), the information from the exposure and toxicity assessments are integrated to characterize risk of lambda-cyhalothrin applications to human health and the environment.

2.0 PROBLEM FORMULATION

Fruit flies in the family Tephritidae are among the most destructive and well-publicized pests of fruits and vegetables around the world. Exotic fruit flies in the genera *Anastrepha*, *Bactrocera*, and *Ceratitis* pose a great risk to U.S. agriculture. Tephritid fruit flies spend their larval stages feeding and growing on over 400 host plants. Introduction of tephritid fruit flies into the United States causes economic losses from destruction and spoiling of host commodities, costs associated with implementing control measures, and loss of market share due to quarantines and restrictions on shipment of host commodities. The extensive damage and wide host range of tephritid fruit flies become obstacles to agricultural diversification and trade when non-native fruit fly species become established in these areas (USDA APHIS, 2013). APHIS PPQ is proposing to use lambda-cyhalothrin to control fruit flies as a replacement for diazinon.

Lambda-cyhalothrin is a restricted-use, broad-spectrum insecticide for controlling most major aphid, caterpillar, and beetle pests on crops as well as public health pests such as mosquitoes and cockroaches in non-agricultural areas. The registered crops include fruits, vegetables, and row and field crops (e.g. alfalfa, corn, cotton, rice, soybean, and winter wheat) (USEPA, 2010a).

Lambda-cyhalothrin is a pyrethroid insecticide (a class of insecticides with a similar structure to pyrethrins, a group of naturally occurring insecticides). Lambda-cyhalothrin penetrates the insect cuticle to disrupt nerve conduction within minutes (NPIC, 2001; He et al., 2008). Lambda-cyhalothrin interferes with the normal functioning of nerve cells by disrupting sodium channels involved in the generation and conduction of nerve impulses leading to cessation of feeding, loss of muscular control, rapid paralysis, and eventual death of an insect (NPIC, 2001; USEPA, 2007; and He et al., 2008).

The following sections discuss the Chemical Description and Product Use; Physical and Chemical Properties; Environmental Fate; and Hazard Identification for Lambda-cyhalothrin.

2.1 Chemical Description and Product Use

Lambda-cyhalothrin (CAS No. 91465-08-6, $C_{23}H_{19}ClF_3NO_3$) is a 1:1 mixture of two stereoisomers, (S)-α-cyano-3-phenoxybenzyl-(Z)-(1R,3R)-3-(2-chloro-3,3,3-trifluoroprop-1-enyl)-2,2-dimethyl cyclopropanecarboxylate and (R)-α-cyano-3-phenoxybenzyl-(Z) -(1S,3S)-3-(2-chloro-3, 3,3-trifluoroprop-1-enyl)-2,2-dimethylcyclopropanecarboxylate. The chemical structures are illustrated in figure 2-1.

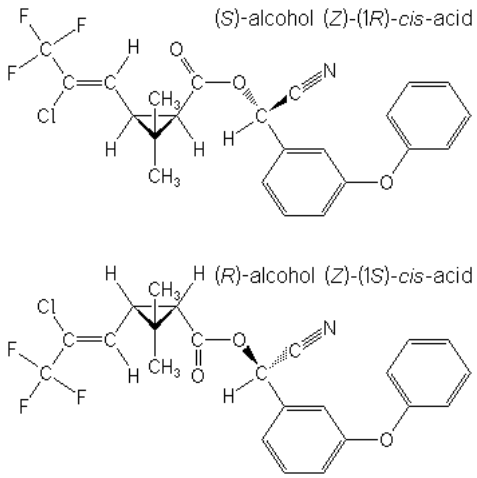

Figure 2-1 The chemical structure of two isomers of lambda-cyhalothrin

First registered with USEPA in 1988, lambda-cyhalothrin is the active ingredient (a.i.) in several brand name products including KARATE®, KARATE ZEON®, ICON®, BESIEGE™, COMMODORE®, DEMAND®, ENDIGO®, ENGEO®, HALLMARK®, MATADOR®, WARRIOR II®, and KUNG FU® (Syngenta, 2015). PPQ is proposing to use a product called Warrior II with Zeon Technology® (Warrior II) (EPA Reg. No. 100-1295) as a soil drench in the fruit fly program. Warrior II is a capsule suspension containing 2.08 lb of active ingredient per gal (22.8% of active ingredient of lambda-cyhalothrin and 77.2% of other ingredients). Other ingredients include titanium dioxide and petroleum distillate. The Warrior II formulation is a restricted use pesticide because of its toxicity to fish and aquatic organisms. It is used only by certified applicators, or persons under their direct supervision, and only for those uses covered by the certified applicator's certification. The application will be performed in accordance with the label conditions for Warrior II and the recent FIFRA Section 24(c) Special Local Need Label (EPA SLN No. FL-150003).

2.2 Physical and Chemical Properties

Lambda-cyhalothrin is a colorless to beige solid with a mild odor (NPIC, 2001). The Warrior II formulation is a white liquid with an aromatic odor (Syngenta, 2010). Lambda-cyhalothrin has a low vapor pressure and Henry's law constant, and has low water solubility. It has a high water–soil organic carbon partition coefficient (Koc) indicating its preferential affinity to organic matter. It also has a high octanol–water partition coefficient (Kow). The physical and chemical properties are summarized in table 2-1.

Table 2-1. Physical and chemical properties of lambda-cyhalothrin.

Parameters	Lambda-cyhalothrin
CAS No.	91465-08-6
Molecular formula	$C_{23}H_{19}ClF_3NO_3$
Molecular weight	449.9
Density (g/mL at 25°C)	1.33
Melting point (°C)	49.2
Boiling point (°C at 0.2 mmHg)	187–190
Henry law constant (Pa-m^3/mole)	0.018
Vapor pressure (mPa at 20°C) (mm Hg at 25°C)	0.0002 (1.5×10^{-9})
Water solubility (mg/L)	0.005
Solubility in solvents such as acetone (mg/L)	500,000
Octanol-water partitioning (log K_{ow} at 20°C)	7.00
Soil adsorption K_{oc} (cm^3/g)	247,000–330,000

Source: He et al., 2008

2.3 Environmental Fate

The environmental fate describes the processes by which lambda-cyhalothrin moves and is transformed in the environment. The environmental fate processes include: 1) mobility, persistence, and degradation in soil, 2) movement to air, 3) migration potential to groundwater and surface water, and 4) plant uptake.

Lambda-cyhalothrin is not mobile and tends to strongly adsorb to organic matter in soil based on its high Koc (ranging between 247,000 and 330,000 cm^3/g). Lambda-cyhalothrin has a low potential to leach as dissolved residues in percolating water because of its low water solubility and high mean Koc. A 28-day leaching study showed that a majority of the lambda-cyhalothrin residues were recovered within the top 15 cm of the soil where the top 10-cm soil layer contained 50 percent clay and 26.3 g/kg organic carbon (Laabs et al., 2000).

In the water column, lambda-cyhalothrin tends to adsorb to suspended particulate materials such as clay particles and organic matter, transport with the suspended particulates through aquatic systems, and settle in the sediments. Sorption of lambda-cyhalothrin to suspended solids or bottom sediments may reduce its short-term bioavailability and mitigate its acute toxicity to aquatic organisms (He et al., 2008).

Lambda-cyhalothrin is considered nonvolatile based on its low Henry's Law constant and vapor pressure (table 2-1). Volatilization of lambda-cyhalothrin from soil and water surfaces occurs slowly. In comparison to soil where lambda-cyhalothrin strongly adheres to soil, volatilization from foliage occurs more rapidly because of the reduced surface area (ATSDR, 2003).

Lambda-cyhalothrin is moderately persistent in the environment. A representative soil half-life for lambda-cyhalothrin is 30 days with values ranging from 28-84 days (NPIC, 2001). Lambda-

cyhalothrin degrades in the environment through a combination of biotic and abiotic mechanisms (photolysis, hydrolysis, and microbial biodegradation) (He et al., 2008; USEPA, 2007). Lambda-cyhalothrin undergoes some photolysis in water, but is somewhat stable in soil (with little degradation, on the order of ~13 percent in 35 days) (USEPA, 2007). Studies show that lambda-cyhalothrin in water and soil when exposed to sunlight photodegrades, with half-lives of 24.5 days (pH 5 and 25^{o}C) and 53.7 days, respectively (He et al., 2008). In water, lambda-cyhalothrin is stable and no hydrolysis occurs at a pH below 8. According to two different authors, it hydrolyzed in water at a pH of 9 with a half-life of approximately 9 days (He et al., 2008) or 13 days (USEPA, 2007). Lambda-cyhalothrin biodegrades at moderate rates (half-lives ranging from 12 to 72 days) under both aerobic and anaerobic soil metabolism conditions. Lambda-cyhalothrin aquatic biodegradation is slow with metabolism half-lives ranging from 113-142 days (USEPA, 2007). Laboratory studies show that the half-lives in aerobic soil and anaerobic aquatic conditions are 42.6 days and 21.9 days, respectively (He et al., 2008). The reported half-lives for lambda-cyhalothrin in soil and water are summarized in table 2-2.

Table 2-2. Reported half-lives for lambda-cyhalothrin in soil and water.

Environmental Fate Parameter	Reported Half-life
Hydrolysis	Stable @ pH 5 and 7, pH 9 (8.66 days)
Soil Photolysis	53.7 days
Aqueous Photolysis	24.5 days @ pH 5 and 25^{o}C
Soil Metabolism Biodegradation (both aerobic and anaerobic)	12 to 72 days
Aquatic Metabolism Biodegradation	113 to 142 days
Aerobic Soil Degradation	42.6 days
Anaerobic Aquatic Degradation	21.9 days

Source: He et al., 2008; USEPA, 2007.

Lambda-cyhalothrin partitions to lipids suggesting a high potential to bioconcentrate due to its high octanol–water partition coefficient (Kow) and low water solubility. The reported bioconcentration factor in fish is 2,240 (He et al., 2008).

Lambda-cyhalothrin in soil is not easily taken up by the roots of vascular plants because it strongly adsorbs to soil (ATSDR, 2003). However aquatic macrophytes can take up lambda-cyhalothrin in water from roots. Through translocation, lambda-cyhalothrin uptake partitions into upper plant biomass. The uptake rates of various macrophytes are species and pesticide specific. Wetlands, detention ponds, and vegetated ditches have shown to be effective mitigation measures to reduce the quantity of runoff and suspended solids (He et al., 2008).

2.4 Hazard Identification

Lambda-cyhalothrin is a hazard to human health due to its neurotoxicity (USEPA, 2017a, 2010b). The neuromuscular system is the main target organ for lambda-cyhalothrin (USEPA 2007). Based on acute oral, dermal and inhalation toxicity, USEPA/OPP classified lambda-

cyhalothrin as moderately toxic (Category II). The eye irritation data shows that it is a moderate eye irritant (Category II), but it is not a skin irritant (Category IV) or a skin sensitizer. Dermal exposure to lambda-cyhalothrin and many other pyrethroids may cause numbness or tingling of the skin (commonly referred as paresthesia).

2.4.1 Toxicological Effects

The primary acute toxic effect of lambda-cyhalothrin is neurotoxicity. Lambda-cyhalothrin inhibits voltage-gated membrane sodium channels of nerve cells from closing. This results in altered nerve function, which manifests either as a series of short bursts or a prolonged burst, and is caused by repetitive discharge of nerve signals or stimulus-dependent nerve depolarization. Only about 0.6 percent of the sodium channel gates need to be affected into order to elicit signs of neurotoxicity (ATSDR, 2003).

2.4.2 Pharmacokinetics

Metabolic studies in rats and dogs show that lambda-cyhalothrin is well absorbed after oral administration, extensively metabolized as a result of ester cleavage to the cyclopropanecarboxylic acid and 3-phenoxybenzoic acid, and eliminated as polar conjugates in urine. Residues in fats were eliminated with a half-life of 23 days (IPCS, 1990). Studies in rats show that lambda-cyhalothrin was widely distributed following both intravenous and oral exposures (Anadon et al., 2006). The highest concentrations were detected in the hypothalamus and the myenteric plexus (i.e., an area of unmyelinated fibers enervating the gastrointestinal tract). The plasma half-lives after intravenous and oral administration in rats were 8.55 and 14.43 hours, respectively. The whole body elimination half-lives after intravenous and oral exposures were 7.55 hours and 10.27 hours, respectively. The half-lives in nerve tissues were substantially greater (12-34 hours) than half-lives in plasma, which is consistent with the mechanism of action of lambda-cyhalothrin and other pyrethroids. An occupational human exposure study reported an average plasma half-life of 6.4 hours for lambda-cyhalothrin and several other pyrethroids (Leng et al., 1997).

2.4.3 Human Incidents

USEPA performed a human incident review based on the OPP incident data system (IDS) and the Centers for Disease Control and Prevention/National Institute for Occupational Safety and Health (CDC/NIOSH) Sentinel Event Notification System for Occupational Risk-Pesticides (SENSOR) database (USEPA, 2010c). The review showed several incidents involving lambda-cyhalothrin. These incidents were low, moderate, and high severity with a majority of the cases from exposure at home using lambda-cyhalothrin products (indoors or outdoors) or under an occupational setting (mixing, loading, applying, or reentering the treated fields, and inadvertent exposure). The most frequently reported symptoms were associated with dermal, respiratory, neurological, gastrointestinal, and ocular systems. The following sections provide more detailed discussions on the human incidents and symptoms identified from each database.

The IDS (2000 to 2010) recorded 403 case reports allegedly attributable to lambda-cyhalothrin. USEPA identified 159 incidents (excluding lawsuits and suicides) that occurred in the United

States from 2007 to April 2010. Symptoms of human exposure to lambda-cyhalothrin reported in the IDS (2007-April 2010) include the following:

1) dermal – itchiness, redness, hives, burning sensation, irritation, and blisters;
2) neurological – headache, dizziness, disorientation, confusion, memory dysfunction, unable to concentrate, numbness, tingling sensations, unsteady movements, muscle weakness, muscle spasms, and seizures;
3) respiratory – coughing, difficulty in breathing, asthma like symptoms, exacerbation of chronic obstructive pulmonary disease, sore throat, burning sensation in the throat, nasal passage and chest, hoarseness of voice, inability to take a deep breath due to chest pain and blood in sputum;
4) ocular – corneal abrasion, sensation of foreign body, burning sensation, pain, photophobia, itchiness, and swelling and redness of eye;
5) gastrointestinal – vomiting, diarrhea, abdominal pain, and stomach cramps;
6) fever, muscle aches, flu-like symptoms; and
7) anaphylactic shock.

The NIOSH SENSOR (1998-2007) reported 217 cases of lambda-cyhalothrin exposure. The USEPA reviewed 159 of these human exposure cases of lambda-cyhalothrin as a single chemical. Among the 159 cases, 145 were of low severity, 14 were of moderate severity, and there were no fatalities. The reported health effects included gastrointestinal, ocular, neurological, dermal, respiratory, and cardiovascular symptoms. Most exposures occurred through drift of the pesticide in indoor and outdoor residential non-occupational situations or in an occupational setting.

USEPA's recent additional review on human incidents and epidemiology (2017) identified numerous lambda-cyhalothrin incidents reported to the Incident Data System (2011–2016) and Sentinel Event Notification System for Occupational Risk-Pesticides (SENSOR)-Pesticides (1998–2013). Less than 1 percent of the cases were classified as having major severity, and there were no deaths reported. The majority of the incidents (96 percent in the Incident Data System and 89 percent in SENSOR-Pesticides) were of minor severity. This means that the symptoms are minimally traumatic, resolved rapidly, and usually involve skin, eye, or respiratory irritation (USEPA, 2017b).

The lambda-cyhalothrin dermal penetration study in humans indicates a dermal absorption estimation of 1 percent, which is much less than the 16 percent dermal absorption estimation in rats (USEPA, 2002). Lambda-cyhalothrin contact with exposed human skin can result in paresthesia (temporary itching, tingling, burning or numbness) at sufficiently high doses. The abnormal skin sensations (tingling, burning, prickling), particularly in the facial region, are unique temporary symptoms of pyrethroid exposure, and the symptoms normally disappear within 24 hours (NPIC, 2001; Syngenta, 2010). Other occupational symptoms reported include nasal and throat irritation for workers who sprayed lambda-cyhalothrin indoors (ATSDR, 2003; Moretto, 1991).

2.4.4 Acute Toxicity

Technical grade lambda-cyhalothrin has moderate acute toxicity (Category II) via oral, dermal, and inhalation routes. The oral median lethal dose (LD_{50}) of the Warrior II formulation is 180 milligrams/kilogram (mg/kg) for female rats based on results from similar products, which is in the same toxicity category as the technical grade. The dermal LD_{50} of the Warrior II formulation is higher than 2,000 mg/kg in rabbits, which has low toxicity (Category III). The inhalation median lethal concentration (LC_{50}) of the Warrior II formulation is 3.12 mg/liter (L) in female rats. Table 2-3 summarizes the acute toxicities for the technical grade and Warrior II formulation. Studies on eye and skin irritation in rabbits show that lambda-cyhalothrin is a mild eye irritant (Category II), but it is not a skin irritant (Category IV) for the technical grade (USEPA, 2002). The Warrior II formulation is moderately skin irritating (Category III). The technical grade is not a dermal sensitizer in the guinea pig. However, the Warrior II formulation is a skin sensitizer (Syngenta, 2010). Skin irritation consistent with paresthesia has been documented in workers handling lambda-cyhalothrin (Spencer and O'Malley, 2006; Moretto, 1991).

Table 2-3. Acute technical and Warrior II formulation lambda-cyhalothrin toxicities for testing mammals.

Toxicity Study	Lambda-cyhalothrin Technical	Warrior II
Acute Oral LD_{50} (rat)	56 mg/kg (♀)/79 mg/kg (♂) (II)	180 mg/kg (♀)* (II)
Acute Dermal LD_{50}	632 mg/kg(♂)/696 mg/kg (♀) (rat) (II)	>2,000 mg/kg (rabbit)* (III)
Acute Inhalation LC_{50} (rat)	0.065 mg/L(♂&♀) (II)	3.12 mg/L (♀)-4 hours (IV)
Primary Eye Irritation (rabbit)	Mild irritant (II)	Mildly Irritating* (II)
Primary Skin Irritation (rabbit)	Not an irritant (IV)	Moderately Irritating* (III)
Dermal Sensitization (Guinea pig)	Not a sensitizer	A skin sensitizer (derived from component)

* The toxicity information for Warrior II was based on results from similar product(s).
Source: USEPA, 2002; Syngenta, 2010.

2.4.5 Subchronic and Chronic Toxicity

A 21-day subchronic dermal toxicity study in rats reported a No Observed Adverse Effect Level (NOAEL) of 10 mg/kg/day and a Lowest Observed Adverse Effect Level (LOAEL) of 50 mg/kg/day, based on clinical signs of neurotoxicity (such as tip-toe gait, and reduced splay reflex), and decreased body weight (USEPA, 2007).

A 21-day subchronic inhalation study in rats reported an inhalation NOAEL of 0.0003 mg/L (0.08 mg/kg/day) and a LOAEL of 0.0033 mg/L (0.90 mg/kg/day) based on clinical signs of neurotoxicity (such as salivation, lacrimation, paw flicking, tail erections), decreased body weight gains, increased incidence of punctate foci in the cornea, slight reductions in cholesterol (female), and slight changes in selected urinalysis parameters (USEPA, 2007). A 28-day subchronic dietary study in mice reported a No Observed Effect Concentration (NOEC) of 500 parts per million (ppm) (64.2 mg/kg bw/day in males and 77.9 mg/kg bw/day in females) and a Lowest Observed Effect Level (LOEL) of 2,000 ppm (≈309 mg/kg bw/day in males and ≈294 mg/kg bw/day in females) (the next higher dietary concentration). At the concentration of 2,000 ppm, signs of neurotoxicity (i.e., abnormal gait and posture) and other effects of toxicity (including weight loss, slight changes in hematology and organ weights) were observed (USEPA, 2007).

In two 90-day subchronic dietary studies using rats, a NOEL of 50 ppm (≈2.5 mg/kg bw/day) and a LOEL of 250 ppm (≈12.4 mg/kg bw/day), based on body weight loss in both studies. Statistically significant decrease in food conversion efficiency was observed in female rats in one of the studies (USEPA, 2007).

The 2-year chronic studies in rats and mice indicate that mice may be more tolerant than rats to dietary administration of lambda-cyhalothrin based on a dietary NOEL of 50 ppm (2.5 mg/kg bw/day) with a LOAEL of 250 ppm (12.5 mg/kg bw/day) in rats, compared to a dietary NOEL of 100 ppm (15 mg/kg bw/day) and a LOAEL of 500 ppm (75 mg/kg bw/day) in mice. The LOAEL for rats is based on decreased body weight with no signs of neurotoxicity. The LOAEL for mice is also based on decreased body weight, piloerection, and abnormal posture in some test animals (USEPA, 2007).

A chronic oral study was performed in dogs by administration of lambda-cyhalothrin in gelatin capsules at doses of 0.1, 0.5, or 3.5 mg/kg bw/day for 1 year. At the lowest dose of 0.1 mg/kg bw/day, no adverse effects were observed. At 0.5 mg/kg bw/day, signs of neurotoxicity (abnormal gait) were observed in some animals from weeks two through nine. At 3.5 mg/kg bw/day, signs of neurotoxicity (ataxia, tremors, convulsions, and vomiting) were observed during the first 2 weeks. Based on this study, USEPA determined the dose of 0.1 mg/kg bw/day as a NOAEL and the dose of 0.5 mg/kg bw/day as a LOAEL for chronic exposures, and the doses of 0.5 mg/kg bw/day as a NOAEL and 3.5 mg/kg bw/day as the LOAEL for acute exposure (USEPA, 2007).

2.4.6 Nervous System Effects

The acute oral neurotoxicity study in rats (USEPA, 2002) administering doses of 2.5, 10, or 35 mg/kg reported a NOAEL of 10 mg/kg and a LOAEL of 35 mg/kg based on clinical signs of neurotoxicity (i.e., piloerection, ataxia, salivation, lacrimation, and decreased motor activity).

The 21-day subchronic dermal and inhalation studies in rats, the 28-day subchronic dietary study in mice, and the chronic oral dog study previously discussed exhibited clinical signs of neurotoxicity.

2.4.7 Reproductive or Developmental Effects

The results of a 3-generation reproduction study in rats testing cyhalothrin at doses of 0, 0.5, 1.5, or 5 mg/kg bw/day showed a NOAEL of 1.5 mg/kg bw/day and a LOAEL of 5 mg/kg bw/day based on a decreased body weight and body weight gain for both parents and offspring. However, no effects were observed in reproductive parameters (i.e., gross signs of toxicity, the length of the estrous cycle, assays on sperm and other reproductive tissue, and the number, viability, and growth of offspring) with a reproductive NOAEL of 5 mg/kg bw/day. There was no evidence of qualitative or quantitative susceptibility observed (USEPA, 2017a).

Developmental studies evaluate the potential to cause birth defects (teratogenic effects) and other effects during development or immediately after birth. The results of the developmental studies for cyhalothrin in both rats and rabbits show no developmental toxicity. At doses of 10 mg/kg bw/day, there were no signs of toxicity. In rats, signs of neurotoxicity and reduced body weight and food consumption were observed in dams (maternal toxicity) at 15 mg/kg bw/day. USEPA reported a NOAEL of 15 mg/kg bw/day based on no effects to the offspring. In rabbits, decreases in body weight and food consumption were noted at 30 mg/kg bw/day. USEPA reported a developmental NOAEL of 30 mg/kg bw/day based on no observed effects to offspring (USEPA, 2002).

Ratnasooriya et al. (2002; 2003) performed two studies on reproductive and developmental effects of lambda-cyhalothrin. One study (Ratnasooriya et al., 2002) reported a decrease in mating behavior in male rats at oral doses about 6.3 and 10 mg/kg bw. The other study (Ratnasooriya et al., 2003) reported a significant increase in embryo implantation losses at 8.3 and 12.5 mg/kg bw/day, with a NOAEL of 6.3 mg/kg bw/day. Dams in the study showed signs of neurotoxicity at all dose levels.

A study conducted in Algeria (Lebaili et al., 2008) reported evidence of testicular damage in rats exposed to very high concentrations (about 15,000 or 23,000 ppm) of lambda-cyhalothrin formulated as KARATE® 2.5 EC in drinking water.

2.4.8 Carcinogenicity and Mutagenicity

USEPA classifies lambda-cyhalothrin as “not likely to be carcinogenic to humans” based on the lack of evidence of treatment related tumors in carcinogencity studies in mice and rats (USEPA, 2002; 2007, 2017a). The chronic feeding/carcinogenicity study of cyhalothrin in rats show that cyhalothrin was not oncogenic under the study conditions (the highest dose in the study was 12.5 mg/kg bw/day). The rat study reported a NOAEL of 2.5 mg/kg/day and a LOAEL of 12.5 mg/kg/day based on decreased body weights (11%). The chronic feeding study of cyhalothrin in mice also show that cyhalothrin was not oncogenic under the study conditions (the highest dose in the study was 75 mg/kg bw/day). The mice study reported a NOAEL of 15 mg/kg/day and a LOAEL of 75 mg/kg/day based on increased incidence of piloerection and hunched posture.

Among eight mutagenicity studies (four studies for technical lambda-cyhalothrin and four studies for technical cyhalothrin) reviewed by USEPA (2002), five studies indicate no mutagenic activity and the other three studies for cyhalothrin are inconclusive because of issues associated

with the experimental designs of the studies. Lambda-cyhalothrin tested negative in all four studies including a reverse mutation assay in *Salmonella typhimurium*, a forward mutation assay in L5178Y mouse lymphoma cells at concentrations below the solubility limit, a mouse micronucleus test in C57B1/6J mice, and an *in vitro* cytogenetics study in human lymphocytes. Cyhalothrin tested negative in one study (a reverse mutation assay in *S. typhimurium*). A study from the open literature using human lymphocyte cultures (Naravaneni and Jamil, 2005) reports that lambda-cyhalothrin was positive in a comet assay (for strand breaks in DNA). Other studies (intraperitoneal injections and oral administration of lambda-cyhalothrin) report chromosome aberrations in rat bone marrow (Celik et al., 2003; 2005a,b). A weak positive mutagenic response (less than threefold of background) at 0.5 to 10 micromole (μmol)/plate was reported in an *in vitro* study assessing lambda-cyhalothrin using the Ames Salmonella assay at doses between 0.125 and 50 μmol/plate (Saleem et al., 2014).

2.4.9 Endocrine System Effects

USEPA (2002) concludes that "There is no evidence that lambda-cyhalothrin induces any endocrine disruption." ATSDR's review (2003) indicated several pyrethroids affect endocrine function, but did not specify lambda-cyhalothrin. Lambda-cyhalothrin is not among the group of 99 pesticide active ingredients on the initial and second lists to be screened under the USEPA Endocrine Disruptor Screening Program. However, the lists of chemicals were generated based on exposure potential, not based on whether the pesticide is a known or likely potential endocrine disruptor (USEPA, 2014). Lambda-cyhalothrin may affect endocrine function based on some published studies in the open literature discussed below.

A 21-day gavage study in rats (Akhtar et al., 1996) showed that serum triiodothyronine (T3), thyroxine (T4) and T3/T4 ratios were significantly suppressed and serum thyroid stimulating hormone levels were significantly increased after administering lambda-cyhalothrin at a dose of approximately 0.73 mg/kg bw/day. No other signs of toxicity or body weight gain were observed at this dose (US FS, 2010).

In an *in vivo* study, pregnant rats were exposed to ICON® (a formulation of lambda-cyhalothrin used in Sri Lanka) by gavage at doses of 6.3, 8.3, or 12.5 mg a.i./kg bw/day for 7 days (Ratnasooriya et al., 2003). The primary adverse reproductive effect observed in this study was increased pre-implantation losses, which was blocked by co-administration of progesterone. The study did not observe effects on birth weight, fetal morphology, pre-natal development, and other standard reproductive parameters.

A study in a breast carcinoma cell line (Zhao et al., 2008) indicated that lambda-cyhalothrin may have estrogenic activity. At concentrations as low as 10^{-7} molar (M) (about 45 micrograms (μg)/L), lambda-cyhalothrin promoted cell proliferation (mimicked the effect of estrogen). Addition of an estrogen receptor antagonist at a concentration of 10^{-9} M blocked the cell proliferation.

2.4.10 Immune System Effects

ATSDR raised concern for the effects of some pyrethroids on immune function as well as neurodevelopmental and reproductive functions at levels below those that induce signs of neurotoxicity (ATSDR, 2003). Two immunotoxicity studies with cyhalothrin (Righi and Palermo-Neto, 2005; Righi et al., 2009) report a decrease in macrophage activity at doses of 1 and 3 mg/kg bw/day but not at 0.6 mg/kg bw/day after an *in vivo* 7-day exposure.

2.4.11 Toxicity of Other Ingredients

Approximately 77 percent of the Warrior II formulation contains other ingredients. Petroleum solvent and titanium dioxide are the two identified ingredients in this category (Syngenta, 2010). However, their percentages are not specified. The Syngenta safety data sheet indicates that the target organs for petroleum solvent are skin, eye, respiratory tract, and central nervous system (CNS). Repeated exposure to petroleum solvent may cause skin dryness or cracking, irritation to the eyes, nose, throat, and lungs, or CNS depression. If swallowed, petroleum solvent may be aspirated and cause lung damage. The safety data sheet also indicated that titanium dioxide is considered "Possibly Carcinogenic to Humans" (IARC Group 2B). The target organ for titanium dioxide is the lung. Prolonged exposure to titanium dioxide causes respiratory irritation and may lead to pulmonary fibrosis.

3.0 DOSE-RESPONSE ASSESSMENT

3.1 Human Health Dose-Response Assessment

A dose-response assessment evaluates the dose levels (toxicity criteria) for potential human health effects including acute and chronic toxicity.

The USEPA/OPP developed an oral Reference Dose (RfD) of 0.005 mg/kg/day for an acute dietary exposure scenario for the general population including infants and children (USEPA, 2002). The acute RfD for lambda-cyhalothrin was derived by applying an uncertainty factor of 100 to the NOAEL of 0.5 mg/kg/day from the chronic oral study in the dog.

The USEPA/OPP uses a benchmark dose (BMD_{1SD}[1]) value of 0.40 mg/kg and a BMD lower confidence limit ($BMDL_{1SD}$[2]) value of 0.28 mg/kg based on decreased locomotor activity from an acute oral study (Moser et al., 2016) to quantify the incidental oral risks for lambda-cyhalothrin. The BMDL value is protective of potential offspring effects that were observed in the 3-generation reproductive toxicity study (USEPA, 2017a).

The USEPA/OPP also derived a chronic RfD of 0.001 mg/kg/day for a chronic dietary exposure scenario for all populations (USEPA, 2002). The chronic RfD for lambda-cyhalothrin was developed by applying an uncertainty factor of 100 to the NOAEL of 0.1 mg/kg/day from a chronic oral study in the dog.

The USEPA/OPP classified lambda-cyhalothrin as “not likely to be carcinogenic to humans” and did not derive a cancer potency factor.

The USEPA established tolerances for the combined residues of lambda-cyhalothrin and its isomers on plants and livestock. The tolerances for pome and stone fruits, which contain species that are hosts of fruit flies, are 0.3 and 0.5 ppm, respectively (40 CFR 180.438).

3.2 Ecological Dose-Response Assessment

3.2.1 Wild Mammal, Avian and Reptile Toxicity

Toxicity data for wild mammal species and lambda-cyhalothrin are not available; however, the data reported in laboratory test mammals can be used as a surrogate for potential effects in acute and chronic exposures. Effects data for mammals is summarized in the previous section discussing toxicity to human health.

Avian toxicity of lambda-cyhalothrin has been characterized in the bobwhite quail and mallard, which are standard surrogate test organisms used in the registration of a pesticide. Dietary LC_{50} values for the mallard and bobwhite quail were greater than 3,948 and 5,300 ppm, respectively

[1] BMD_{1SD} is the central estimate of the dose that results in decreased motor activity compared to control animals based upon 1 standard deviation using Benchmark Dose Analysis.
[2] $BMDL_{1SD}$ is the 95% lower confidence limit of the central estimate.

(USEPA, 2015). The only oral LD_{50} study was for the mallard with a reported median lethality value of greater than 3,150 mg/kg. Available oral and dietary dosing studies suggest lambda-cyhalothrin is practically non-toxic to birds. Chronic reproduction studies report NOECs of greater than 30 and 50 ppm for the bobwhite and mallard, respectively (USEPA, 2015).

No reptile toxicity data for lambda-cyhalothrin appears to be available based on a search of the available literature and databases. USEPA/OPP assumes that avian toxicity is similar to reptile toxicity in their risk assessment process. There is uncertainty in this assumption based on differences between the two taxa; however, due to the lack of data, the same assumption is being made in this assessment.

3.2.2 Terrestrial Invertebrate Toxicity

Lambda-cyhalothrin is considered highly toxic to most terrestrial invertebrates, including pollinators. The acute contact LD_{50} for the honeybee is 0.038 µg/bee and the oral LD_{50} in oral studies is 0.91 µg/bee, suggesting lambda-cyhalothrin is highly toxic to honeybees (USEPA, 2006). Based on the proposed use pattern for lambda-cyhalothrin, soil invertebrates would be the most likely non-target terrestrial invertebrates to be exposed after treatment. Soil arthropods are more sensitive to lambda-cyhalothrin than earthworms based on available data (Frampton et al., 2006). The reported hazard concentration that would impact five percent (HC_{05}) of the soil invertebrate fauna was estimated to be 0.09 mg/kg dry soil. Garcia et al. (2008) reported a range of acute and sublethal effects to the earthworm, *Eisenia foetida*, based on various soil types. Reported LC_{50}/NOECs ranged from 23.9 and 10 ppm in tropical soils, to 139.9 and 31.6 in European soils.

3.2.3 Terrestrial Plant Toxicity

No terrestrial phytotoxicity data appears to be available for lambda-cyhalothrin. USEPA/OPP does not typically require phytotoxicity information to be collected for the registration of insecticides. The mode of action for lambda-cyhalothrin suggests that toxicity would be low. In addition, lambda-cyhalothrin has a variety of agriculture and non-agricultural uses and there is no information from those uses that would demonstrate impacts to target crops where it has been applied.

3.2.4 Aquatic Toxicity

Lambda-cyhalothrin is considered very highly toxic to aquatic vertebrates and invertebrates. Representative toxicity data for warm water and cold water fish species show typical median lethality values ranging from 0.078 to 7.92 µg/L (USEPA, 2015; Kumar et al., 2011; US FS, 2010) (table 3-1).

Table 3-1. Representative toxicity of lambda-cyhalothrin to fish.

Common Name	Scientific Name	LC_{50} (µg/L)	NOEC (µg/L)
Bluegill sunfish	*Lepomis macrochirus*	0.21	0.10
Rainbow trout	*Oncorhynchus mykiss*	0.19-0.24	0.03-0.051
Golden orfe	*Leuciscus idus*	0.078	0.055
Channel catfish	*Ictalurus punctatus*	0.16	NR
Fathead minnow	*Pimephales promelas*	0.70	NR
Sheepshead minnow	*Cyprinodon variegatus*	0.807	0.29
Carp	*Cyprinus carpio*	0.50	NR
Three-spined stickleback	*Gasterosteus aculeatus*	0.40	NR
Guppy	*Poecilia reticulata*	2.2	NR
Catfish	*Clarias batrachus*	5.1	NR
Catfish	*Channa punctatus*	7.92	NR

NR = Not reported

Acute toxicity data for lambda-cyhalothrin and amphibians is limited to a *Rana* species where the 48-hour LC_{50} was reported as 4 µg/L (Pan and Liang, 1996). Saghir et al. (2014) noted changes in the gonads of adult frogs exposed to lambda-cyhalothrin at concentrations ranging from 8 to 12 µg/L. The species was not given in the study and it should be noted the dosing levels were above median lethality values for fish.

Chronic toxicity to fish is also high with a reported NOEC of 0.25 µg/L in an early life stage study using the sheepshead minnow, and a NOEC of 0.031 µg/L in a fish full life cycle study using the fathead minnow (USEPA, 2006).

Toxicity to freshwater and marine aquatic invertebrates is also high with EC/LC_{50} values ranging from the low parts per trillion to low parts per billion range (USEPA, 2015, Maund et al., 1998) (table 3-2). Chronic toxicity is also high with a reported NOEC 0.002 µg/L for the cladoceran, *D. magna* in 21-day reproduction study (Maund et al., 1998).

The range of effects concentrations for aquatic invertebrates that have been established in laboratory studies have also been observed in lambda-cyhalothrin-dosed microcosm and mesocosm studies that have been summarized in the literature (US FS, 2010; Van Wijngaarden et al., 2005).

The low water solubility and strong binding affinity of lambda-cyhalothrin can reduce the bioavailability and toxicity to aquatic organisms (Maund et al., 1998; Hamer et al., 1999).

Table 3-2. Aquatic toxicity of lambda-cyhalothrin to aquatic invertebrates.

Common Name	**Scientific Name**	**LC_{50}/EC_{50} (ug/L)**
Amphipod	*Gammarus pulex*	0.0014-0.0068
	Hyallela azteca	0.0023
Phantom midge	*Chaoborus sp.*	0.0028
Mosquito	*Culex tritaeniorhynchus*	0.001
Cladoceran	*Daphnia magna*	0.051-0.23
Mysid	*Americamysis bahia*	0.0041
Water hoglouse	*Asellus aquaticus*	0.026
Water boatman	*Corixa sp.*	0.030
Mayfly	*Cloeon dipterum*	0.038
Water mite	*Hydracarina*	0.047
Damsel fly	*Ischnura elegans*	0.13
Pacific oyster	*Crassostrea gigas*	>590

4.0 EXPOSURE ASSESSMENT

4.1 Human Health Exposure Assessment

The exposure assessment estimates the potential exposure of humans to lambda-cyhalothrin. The exposure assessment begins with the use and application method for lambda-cyhalothrin in the fruit fly program. A complete exposure pathway for lambda-cyhalothrin includes (1) a release from a lambda-cyhalothrin source, (2) an exposure point where contact can occur, and (3) an exposure route such as ingestion, inhalation, or dermal contact. In this way, the potentially exposed human populations and complete exposure pathways are identified. Finally, exposures for the identified human populations are qualitatively and quantitatively evaluated for each exposure pathway.

4.1.1 Identification of Potentially Exposed Human Populations and Complete Exposure Pathways

Lambda-cyhalothrin in the Warrior II formulation is applied as a soil drench. Drift from the soil drench application is minimal because large coarse droplets are applied in close proximity to the targeted area. Based on the application method, workers (i.e., certified applicators or persons under their direct supervision) in the program are the most likely human population segment to be exposed to lambda-cyhalothrin. The potential exposure pathways for these workers include direct contact (i.e., incidental ingestion, inhalation, and dermal contact) to lambda-cyhalothrin during application. However, direct contact exposures are minimized with the use of personal protective equipment (PPE). Accidental exposure may occur from splash or transfer from contaminated gloves or clothing to an unprotected skin area (face). The occurrence for accidental exposure is unlikely with well-trained certified applicators.

By providing adequate notice about a planned treatment program, as specified in the FIFRA Section 24(c) Special Local Need Label (Syngenta, 2014), the general public (e.g., residents) are not recognized as a potentially exposed segment of the human population. APHIS will notify residents whose property will be treated with soil drenches in writing 24 hours prior to treatment. With the notification to the public in place, potential residential exposure to lambda-cyhalothrin is very low. The label requires applications to be made by or under the supervision of a licensed state or federal employee with the following specifics to prevent the pesticide mixture to remain on the surface of the treated areas:

- pre-drench areas prior to the pesticide application with sufficient water (up to 20 gallons per 1000 sq. ft.) to break the surface tension of soil to allow adequate penetration of the pesticide mixture;
- make treatments to ensure that no surface liquid remains in order to avoid non-target exposure of humans, animals, and nontarget species; and
- remain on-site until the application has been absorbed into the soil when absorption is slow.

A complete exposure pathway associated with direct contact to lambda-cyhalothrin from the soil drench application is not identified for the general public. There is the potential for a child to be

exposed to lambda-cyhalothrin in treated soil via pica behavior (a pattern of eating non-food materials, such as dirt or paper) generally seen in young children. Ten to 32 percent of children ages 1 to 6 exhibit this type of behavior (MedlinePlus, 2014). In this exposure scenario, the potential exposure for a child is expected to be limited because families would be notified of treatments on residential properties. However, as a conservative approach, the potential exposure and risk for this unusual exposure scenario are further quantified.

A complete exposure pathway is not identified for dietary consumption of fruit from treated fruit bearing trees. Lambda-cyhalothrin applied through soil drench is unlikely to be taken up by the roots of vascular plants and be present in any fruit (see Section 2.3). Second, APHIS will remove and destroy all fruit from fruit-bearing host plants where soil drench applications were made, eliminating dietary exposure to lambda-cyhalothrin.

A complete exposure pathway is not identified for the groundwater medium. Lambda-cyhalothrin has low water solubility and adsorbs strongly to soil (see Section 2.3). As a result, leaching into groundwater from soil by the soil drench application is not expected.

A complete exposure pathway is not identified for the surface water medium. Significant surface runoff is not expected to occur from the soil drench application based on program and label requirements on application buffers near water bodies, and the presence of a vegetative buffer strips, as well as the reported low mobility for lambda-cyhalothrin.

4.1.2 Exposure Evaluation

This section qualitatively evaluates worker exposure from direct contact pathways while mixing and applying lambda-cyhalothrin based on the application rate for the soil drench scenario. The section also quantitatively evaluates the potential exposure to lambda-cyhalothrin in soil for a child from the unusual soil ingestion behavior (pica).

Under the FIFRA Section 24(c) label, the application rate is a single maximum rate of 0.0092 lb a.i. per 1000 sq. ft. of soil surface (equals 0.56 fl. oz. of product in 15.5 gallon of water per 1000 sq. ft). The Warrior II product is mixed in the field (0.73 fl. oz. product in 20 gallons of water to form a solution/suspension). The pesticide mixture is applied within the drip line of fruit-bearing host plants that are located within a 400-meter radius from a non-native fruit fly larval, pupal, egg, or mated female find. It is also applied as a regulatory treatment to host nursery stock and to soil around nursery stock to allow nursery stock to move within and out of the quarantine area.

Direct contact to lambda-cyhalothrin during application is not expected to occur with proper worker hygiene and properly functioning PPE. The PPEs for applicators and other handlers as specified on the label include a long-sleeved shirt and long pants, chemical-resistant gloves (Category G, such as barrier laminate or Viton® > 14 mils), shoes plus socks, and protective eyewear. Lambda-cyhalothrin has a low vapor pressure and low Henry's law constant, and is not volatile. A respirator is not required for handling this product for commercial applications and/or on-farm applications because the potential for inhalation exposure is unlikely. For the manufacture, formulation, and packaging of the product, Syngenta in the material safety data sheet (Syngenta, 2010) recommends the use of effective engineering controls to comply with the

occupational exposure limit (i.e., Syngenta Occupational Exposure Limit (OEL) of 0.04 mg/m^3 TWA (skin) for lambda-cyhalothrin).

To quantify the potential exposure to lambda-cyhalothrin in soil for a child from pica, an upper bound soil concentration was estimated using the label application rate for a soil drench scenario based on the following assumptions:

- A single maximum rate of 0.0092 pounds of lambda-cyhalothrin per 1000 square ft of soil surface from the Warrior II 24(c) label;
- Top 1 inch of soil depth containing lambda-cyhalothrin based on 0.5 to 1 inches of soil drench; and
- Default soil bulk density of 1.4 g/cm^3 for sandy loams and loams soil type (USDA NRCS, 2014)

Acute and chronic exposure intake values were calculated using the following USEPA soil ingestion exposure intake equations:

> Acute Exposure Intake = (Soil Concentration x Soil Ingestion Rate) / (Body Weight)
>
> Chronic Exposure Intake = (Soil Concentration x Soil Ingestion Rate x Exposure Duration x Exposure Frequency x Conversion Factor) / (Averaging Time x Body Weight) (USEPA, 2002).

Information on exposure parameters such as soil ingestion rate, exposure duration, exposure frequency, averaging time, and body weight, and calculated acute and chronic exposure intake values are presented in appendix A. The calculated acute and chronic exposure intake values are included in the risk summary table (table 5-1) in Section 5.1.

4.2 Ecological Exposure Assessment

4.2.1 Terrestrial Exposure Assessment

Exposure to terrestrial vertebrates such as wild mammals, birds, and reptiles is expected to be minimal. Lambda-cyhalothrin applications occur to soil under the drip line of trees or to containerized plants within nurseries that are under quarantine. Wild mammals, birds, and reptiles would not be expected to forage exclusively in containerized plants. In other cases where a treatment is made to a fruit fly host tree within 400-m of a fruit fly detection, these applications are made only to soil within the dripline of the host tree, resulting in a low probability of exposure. There is the potential for terrestrial vertebrates to forage under these trees for soil borne invertebrates where they could consume treated soil and soil invertebrates that may contain lambda-cyhalothrin residues. However, based on the typical food consumption rate for various sized mammals, birds, and reptiles, and the toxicity profile for lambda-cyhalothrin, there is not a plausible exposure scenario where they would consume lambda-cyhalothrin residues from soil or soil borne invertebrates that could result in adverse effects.

Significant exposure to pollinators, such as honey bees is also not expected because lambda-cyhalothrin is being applied directly to soil and not to flowering parts of host trees. Lambda-cyhalothrin is not systemic and soil applications would not result in detectable levels of lambda-cyhalothrin in pollen and nectar. There is the potential for exposure to soil borne terrestrial invertebrates. Upper limit estimated soil residues are 1.3 mg/kg based on conservative assumptions regarding application rates (appendix A).

4.2.2 Aquatic Exposure Assessment

Aquatic exposure is expected to be low for the proposed use of lambda-cyhalothrin in the fruit fly program based on the proposed use pattern and label restrictions designed to protect water quality. Applications are made directly to soil to individual trees within the 400-m radius of a non-native fruit fly detection, or to containerized plants that are located in nurseries under quarantine. The method of application reduces the chance of any significant drift from these applications and the environmental fate and label restrictions will reduce runoff. Lambda-cyhalothrin has low water solubility and a high binding affinity for soil and sediment which will reduce runoff. Material that is not bound to soil or organic matter will preferentially bind to sediment once it enters water, reducing the bioavailability and risk to water column non-target aquatic species. Current label requirements regarding application buffers near water bodies, and the presence of a vegetative filter strip will further reduce the potential for significant aquatic residues. These mitigation measures have been shown to be beneficial for reducing runoff of pesticides, including lambda-cyhalothrin (Moore et al, 2001; He et al., 2008).

5.0 RISK CHARACTERIZATION

5.1 Human Health

Risks associated with adverse human health are characterized qualitatively and quantitatively in this section. Under the APHIS proposed applications, the use of lambda-cyhalothrin for the fruit fly eradication program should pose minimal risks to human health.

Exposure to lambda-cyhalothrin via oral, inhalation, and dermal routes is expected to be minimized by workers (i.e., certified applicators) adherence to the label required PPE. Although lambda-cyhalothrin is a hazard to humans because of its acute toxicities via the oral, inhalation, and ocular routes, the low potential for exposure to lambda-cyhalothrin suggests that adverse health risk to workers is not expected. Accidental exposure from splash to unprotected body areas may occur. The exposure frequency is considered low for this exposure scenario because only certified applicators working with State and Federal agencies, or person under their guidance, will be making applications in the fruit fly program. Therefore, risk from accidental exposure is minimal.

The risks to the public associated with potential exposure to lambda-cyhalothrin during soil drench applications, and dietary consumption of fruit from the treated fruit-bearing trees are low based on notification of the public and destruction of fruit in treated areas. Pica behavior is reported in only 10 to 32 percent of children ages 1 to 6. Consequently, the risks associated with residential children accidentally being exposed to treated soil through pica behaviors are low because children of this age and with this disorder primarily are under adult supervision.

To quantify the risk from child (age 1-6) exposure to soil from pica behavior, hazard quotients (HQs) were calculated using the following USEPA soil ingestion risk estimation equation for non-carcinogens:

Acute HQ = Acute Exposure Intake / Reference Dose

Chronic HQ = Chronic Exposure Intake / Reference Dose (USEPA, 2002).

Only non-cancer risks were evaluated because USEPA classified lambda-cyhalothrin as “not likely to be carcinogenic to humans”. The calculated acute and chronic HQ values (table 5-1) were below the USEPA’s level of concern (HQ=1) suggesting minimal risk to lambda-cyhalothrin exposure from soil ingestion behavior (pica) by children. The risk calculation sheets are included in appendix A.

Table 5-1. Hazard quotients estimated for child exposure to soil from pica behavior.

Parameter	Upper Estimation
Estimated soil concentration	1.3 mg/kg
Acute exposure intake	8.4E-04 mg/kg-day
Chronic exposure intake	1.9E-04 mg/kg-day
Acute reference dose	0.005 mg/kg-day
Chronic reference dose	0.001 mg/kg-day
Acute HQ	0.17
Chronic HQ	0.19

5.2 Terrestrial and Aquatic Risk Characterization

The risk of lambda-cyhalothrin use to non-target terrestrial vertebrates is expected to be very low. Available toxicity data for mammals and birds and the proposed use pattern suggest that the probability of exposure to a significant amount of lambda-cyhalothrin that would result in adverse effects is very low. Primary exposure and risk for terrestrial vertebrates would be through the consumption of treated soil and any associated soil invertebrates. The low frequency of these treatments in the program, the targeted application to soil in either containerized plants or the drip line of host trees in a small area, suggest that non-target birds and mammals would have to consume many times their daily food consumption rates to receive a dose that could result in an effect. Indirect effects through loss of prey items for insectivores is also not expected because applications are targeted to either containerized plants, where non-target mammals and birds would not forage solely or to small areas under the drip line of host trees. These treatments and their frequency of use in the program would not result in significant terrestrial invertebrate population declines that could impact prey consumption by insectivorous mammals and birds. Lambda-cyhalothrin would be expected to impact some soil borne terrestrial invertebrates. The HC_{05} of 0.09 mg/kg is below the estimated upper level lambda-cyhalothrin concentrations that were calculated in the human health soil exposure exercise (1.3 mg/kg). The exposure estimate is below available earthworm acute and chronic exposure endpoints suggesting that impacts to soil invertebrates would be mostly to sensitive arthropods. Any impacts would be limited to directly below the drip line where applications are being made and are not expected to have impacts over a large area.

Lambda-cyhalothrin is highly toxic to aquatic biota; however, the use pattern in the fruit fly program, the low frequency of use in the program, and the associated current label restrictions that require protection of aquatic areas are expected to result in low risk to aquatic vertebrates and invertebrates. In addition, the method of application reduces off-site transport from drift, and any transport would occur from runoff. Lambda-cyhalothrin in runoff would be adsorbed to soil particles, and other organic matter, further reducing its availability to water column aquatic fauna. Exposure and risk would be greatest for aquatic biota that use or occupy the sediment in an aquatic habitat; however, these risks are expected to be low.

6.0 UNCERTAINTIES AND CUMULATIVE IMPACTS

The uncertainties associated with this risk evaluation arise primarily from lack of information about the effects of lambda-cyhalothrin, its formulations, metabolites, and potential mixtures to non-target organisms that can occur in the environment. These uncertainties are not unique to this assessment but are consistent with uncertainties in human health and ecological risk assessments with any environmental stressor. In addition, there is uncertainty in where an exotic fruit fly in the United States and the extent of lambda-cyhalothrin use in a given infestation because its use is based on site-specific factors. Exotic fruit fly outbreaks are periodically events, which occur in various locations and rarely occur in the same location each year.

Another area of uncertainty is the potential for cumulative impacts to human health and the environment from the proposed use of lambda-cyhalothrin in the fruit fly eradication programs. Areas where cumulative impacts could occur are: 1) repeated worker and environmental exposures to lambda-cyhalothrin from program activities in conjunction with other crop use sources; 2) co-exposure to other chemicals with a similar mode of action; and 3) exposures to other chemicals in mixtures and how that may affect the toxicity of lambda-cyhalothrin.

Temporal variability in the occurrence of multiple stressors, as well as their effects, is not well understood. As an example, available water quality monitoring data in the United States indicate the presence of multiple natural and anthropogenic contaminants. Sources for these chemicals can occur from point and non-point sources, and the relative contribution from each is dependent on land use in a given watershed. Based on the most recent United States Geological Survey National Water Quality Assessment (USGS–NAWQA) data for pesticides, frequency of occurrence for two or more pesticides in surface water exceeds 80 percent nationally (Gilliom et al., 2006). When considering other organics and trace metals, the combination of mixtures can become extremely large, especially when spatial and temporal variability in mixtures that can occur in a given watershed are considered. The seasonal variability in mixtures of pesticides and other contaminants has been well documented nationally in urban and agricultural areas (Ryberg et al., 2010; Gilliom et al., 2006; Stone et al., 2014). An analysis of all detections from agricultural streams indicated more than 6,000 unique mixtures of 5 pesticides (Gilliom et al., 2006). Pyrethroid insecticides, including lambda-cyhalothrin, have been identified as a component of these mixtures in water/sediment monitoring data in both urban and agricultural settings (Weston et al, 2004; 2009; 2011; Hintzen et al., 2009). As would be expected, based on the large variability in mixtures, the ecological and human health response data for these types of exposure scenarios is very limited for all organic and inorganic chemicals including those proposed in the program.

Cumulative impacts may occur from lambda-cyhalothrin use from other APHIS programs and in relation to other chemicals that have a similar or different mode of action, and can result in synergism, potentiation, additive, or antagonistic effects. The potential for co-exposure to other pesticides within the program with the same toxic action is not expected. The other pesticide used in the fruit fly eradication program is spinosad. Spinosad over-activates the central nervous system of insects via the nicotinic acetylcholine receptors. Lambda-cyhalothrin disrupts normal nerve function by inhibiting the closing of the voltage-gated membrane sodium channels of nerve cells. Lambda-cyhalothrin contains a cyano group (i.e., a carbon-nitrogen triple bond) and

is structurally considered a Type II pyrethroid. The neurotoxicity of lambda-cyhalothrin is similar to other commonly used Type II pyrethroids such as gamma-cyhalothrin, cyfluthrin, cypermethrin, deltamethrin, esfenvalerate, fenvalerate, fenpropathrin, flucythrinate, flumethrin, fluvalinate, and tralomethrin (ATSDR, 2003). However, the fruit fly program does not use any of the other Type II pyrethroids. Non-APHIS uses of lambda-cyhalothrin include food and non-food crop uses such as indoor and outdoor use in homes, hospitals, and other buildings; greenhouse, ornamental plant, and lawn treatments; insecticide treatments for cattle; termite treatments; and right-of-ways (NPIC, 2001). Cumulative impacts from lambda-cyhalothrin is expected to be incrementally minor due to the proposed use pattern of lambda-cyhalothrin in the exotic fruit fly program.

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Appendix A
Risk Estimates for Soil Ingestion in Children (ages 1-6) with Pica

Appendix A includes equations and assumptions used for risk estimations of soil ingestion in children (ages 1-6) with pica behavior.

Equations:
Acute Exposure Intake = (C x IR) / BW
Chronic Exposure Intake = (C x IR x ED x EF x CF) / (AT x BW)
Hazard Quotient (HQ) = Exposure Intake / RfD

Where:

Exposure Intake – mg/kg/day
HQ - unitless
C – Soil concentration (mg/g)
IR – Ingestion rate (g/day)
BW – Body weight (kg)
ED – Exposure duration (year)
EF – Exposure frequency (days/year)
CF – Conversion factor (kg/mg)
AT – Averaging time (days)
RfD – Reference dose (mg/kg/day)

Assumptions for soil concentration estimation: Based on the Warrior II 24(c) label, a single maximum rate of 0.0092 pounds of lambda-cyhalothrin per 1000 square ft of soil surface was used for the soil concentration calculation.

Parameters	**Input Values**
Amount of lambda-cyhalothrin per 1000 ft^2	0.0092 lb (4173.0464 mg)
Soil surface area	1000 ft^2
Depth of surface soil (assumed top 1 inch)	1 inch (0.083 ft)
Soil volume (soil surface area x depth)	83.3333 ft^3 (2359736.27 cm^3)
Soil bulk density*	1.4 g/cm^3
Soil weight (soil volume x density)	3303.63078 kg
Estimated soil concentration (mg a.i./kg soil)	1.3 mg/kg

* Default soil bulk density for sandy loams and loams (USDA NRCS, 2014)

Assumptions for risk estimation:

Parameters	Upper Estimates	Sources
Estimated soil concentration (mg/kg)	1.3	Calculated
Acute Ingestion Rate (IRa) g/day	10	USEPA, 2002
Chronic Ingestion Rate (IRc) mg/day	1000	USEPA, 2011
Exposure Duration (ED) year	6	USEPA, 2011
Exposure Frequency (EF) (days/year)	84	Biodegradation time for lambda-cyhalothrin in soil without vegetation (NPIC, 2001)
Conversion Factor (CF) (kg/mg)	1.00E-06	USEPA, 2002
Averaging Time (AT) (days)	2190	USEPA, 2002
Body Weight (BW) (kg)	15	USEPA, 2002
Acute Exposure Intake (mg/kg-day)	8.4E-04	Calculated
Chronic Exposure Intake (mg/kg-day)	1.9E-04	Calculated
Acute Reference Dose (RfD) (mg/kg-day)	0.005	USEPA, 2002
Chronic Reference Dose (RfD) (mg/kg-day)	0.001	USEPA, 2002
Acute Hazard Quotient (HQ)	**0.17**	calculated
Chronic Hazard Quotient (HQ)	**0.19**	calculated