United States Department of Agriculture

Marketing and Regulatory Programs

Animal and Plant Health Inspection Service

Human Health and Ecological Risk Assessment for STATIC™ Spinosad ME Bait Applications

March 2014

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EXECUTIVE SUMMARY

USDA APHIS Plant Protection and Quarantine (PPQ) is proposing to use a new formulation of spinosad in its fruit fly eradication program. Spinosad is currently used in the program however there is a need to develop a new formulation with increased efficacy and as a potential replacement for a similar formulation that uses the organophosphate insecticide naled. The proposed formulation STATIC™ Spinosad ME contains the insecticide spinosad, as well as the attractant methyl eugenol, which is designed to attract and kill, male fruit flies.

USDA APHIS evaluated the potential human health and ecological risks from the proposed use of STATIC™ Spinosad ME in this assessment and determined that the risks to human health and the environment are negligible. The lack of risk to human health and the environment is based on the low probability of exposure to human health and the environment and favorable environmental fate and effects data. The method of application for STATIC™ Spinosad ME is by hand as dollops or large droplets to sites on telephone poles, light poles, fences, other inanimate objects, non-crop tree trunks or limbs and non-edible foliage. The proposed method of application substantially reduces the potential for exposure to human health and the environment, such as nontarget fish and wildlife. Risks to workers and the general population are expected to be minimal based on the labeled use, lack of application to food crops, and a favorable toxicity profile when considering acute or chronic effects. Risks to nontarget fish and wildlife are also anticipated to be negligible based on the proposed use pattern resulting in a low potential for exposure to most taxa. A favorable environmental fate profile and low toxicity to most nontarget organisms further reduces the risk to terrestrial and aquatic animals.

1.0 INTRODUCTION

USDA APHIS is proposing to use a new formulation of spinosad, STATIC™ Spinosad ME, in its fruit fly eradication program. This product has been shown to effectively control fruit flies and is intended to supplement other uses of spinosad in the program and may reduce the need for naled, an organophosphate insecticide, in its male annihilation technique (MAT) applications (Vargas et al. 2003, 2009). USDA APHIS has previously assessed the human health and ecological risks of spinosad under different formulations and use patterns however with the proposed new formulation there is a need to determine if this specific formulation and use pattern will pose a risk beyond what has been determined in previous assessments (USDA APHIS1999, 2003).

This human health risk assessment (HHRA) and ecological risk assessment (ERA) provide a quantitative and qualitative evaluation of the potential risks and hazards to human health and non-target fish, and wildlife as a result of exposure to spinosad under the proposed bait applications of STATIC™ Spinosad ME.

The methods used in this HHRA follow standard regulatory guidance and methodologies (NRC 1983, USEPA 2013a), and generally conform to other Federal agencies such as U.S. Environmental Protection Agency, Office of Pesticide Programs (USEPA/OPP). The methods used to assess potential ecological risk to nontarget fish and wildlife follow EPA methodologies regarding eco-risk assessment, with an emphasis on those used by USEPA/OPP in the pesticide registration process.

The following risk assessment is divided into four sections: problem formulation (identifying hazard), exposure assessment (identifying potentially exposed populations and determining potential exposure pathways for these populations), toxicity assessment (the dose-response assessment), and the integration of the exposure and toxicity assessments, or risk characterization.

2.0 PROBLEM FORMULATION

Fruit flies in the family Tephritidae are among the most destructive pests of fruits and vegetables around the world. The genera Anastrepha, Bactrocera, and Ceratitis pose the greatest risk to U.S. agriculture. Tephritid fruit flies spend their larval stages feeding and growing in over 400 host plants. Introduction of these pest species into the United States causes economic losses from destruction and spoiling of host commodities by larvae, costs associated with implementing control measures, and loss of market share due to 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 pest fruit fly species become established in these areas (USDA APHIS 2013).

Spinosad is a broad spectrum insecticide registered for use on agricultural crops, ornamentals, tree farms/plantations, turfgrass, home gardens and lawns (residential use). It is also registered for drywood termiticide use, poultry use, area-wide fruit fly use, post-harvest grain use, larval mosquitoes, and as a seed treatment (USEPA 2011).

In the USDA APHIS Fruit Fly Eradication Program, spinosad and the attractant, methyl eugenol, are used in combination as a bait to control multiple species of tephritid fruit flies that infest tree, vine and vegetable crops. The bait is a thick yellow-brown liquid with a sweet fruit odor. Fruit flies can detect the bait several yards away from the deposition site. Through ingestion. spinosad over-activates the central nervous system of insects via the nicotinic acetylcholine receptors. Target insects exhibit tremors, trembling, paralysis and eventual death. APHIS PPQ proposes to use STATIC™ Spinosad ME bait for its programs.

The following sections discuss the chemical description and product use of STATIC™ Spinosad ME; physical and chemical properties; environmental fate; and hazard identification for spinosad and methyl eugenol.

2.1 Chemical Description and Product Use

STATIC™ Spinosad ME is an insecticidal bait containing 2% spinosad (active ingredient) and 51% methyl eugenol (a chemical attractant) dispersed within a waxy formulation carrier (SPLAT™). Spinosad is a mixture of spinosyn A and D (macrocyclic lactones). The formulation is in a ratio of 85:15 of spinosyn A to D. Spinosad is produced biologically from the fermentation culture of the actinomycete *Saccharopolyspora spinosa*, a bacterial organism isolated from soil.

STATIC™ Spinosad ME is used for selective attraction and control of male tephritid fruit files of the genus *Bactrocera* (or other fruit fly species which respond to the male specific attractant methy eugenol). The product selectively eliminates male fruit flies from a localized area, which disrupts mating leading to decline or local eradication of a fruit fly population. It is most effective when fruit fly populations are maintained at low levels and males are already scarce.

The preferred application method is as small dollops or large droplets targeted as spot applications to stakes, posts, fences, non-crop tree trunks or limbs, artificial targets, or non-edible border vegetation surrounding crop fields. The proposed use of this new formulation is similar where it will be applied by hand in dollops to sites on telephone poles, light poles, fences, other inanimate objects, non-crop tree trunks or limbs, non-edible foliage where it won't be readily accessible to the general public. The application techniques can vary from application of dollops using a spatula or other spreading implement to mechanical or pneumatic meter-jet capable of delivering large droplets. Aerial applications are not permitted.

The product comes as a ready-to-use formulation. The application rates of this formulation for spot applications to non-crop surfaces are 3.4 to 6.85 fl oz (0.0045 to 0.009 lb) active ingredient (ai) spinosad per acre.

2.2 Physical and Chemical Properties

Spinosad (technical grade) is a light gray to white crystalline solid with an odor of slightly stale water (CDPR 2002). The chemical structure of spinosad is shown in Figure 2-1.

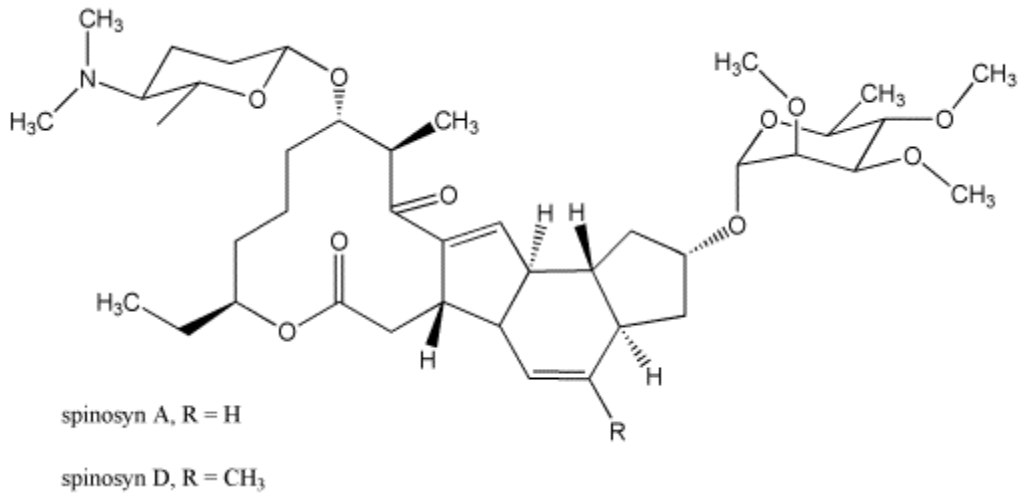

Figure 2-1 Spinosad: Spinosyn A + Spinosyn D

The physical and chemical properties of spinosad are summarized in Table 2-1. Spinosad has low volatility potential based on its low vapor pressure and Henry's Law Constant values.

Table 2-1 Physical and Chemical Properties of Spinsad

Common Name	Spinosad		Reference
Chemical Name	Spinosyn A	Spinosyn D	
Molecular formula	$C_{41}H_{65}NO_{16}$	$C_{42}H_{67}NO_{16}$	CDPR 2002
CAS No.	131929-60-7	131929-63-0	CDPR 2002
Melting point	84°C to 99.5°C	161.5 °C to 170°C	USEPA 1997
Vapor pressure (25°C)	3.0×10^{-11} hPa 2.4×10^{-10} mm Hg	2.0×10^{-11} hPa 1.6×10^{-10} mm Hg	USEPA 1997 Cleveland et al. 2002
Octanol-water Partition Coefficient (Kow)	54.6	90	CDPR 2002
Partition coefficients (log Kow) at 23°C	pH 5: 2.8 pH 7: 4 pH 9: 5.2	3.2 4.5 5.2	USEPA 1997
Henry's Law Constant (Kh) at 25 °C, pH 7	9.82×10^{-10} atm-m^3/mol	4.87×10^{-7} atm-m^3/mol	CDPR 2002
Water solubility	89.4 ppm 290 to 16 mg/L with increasing pH	0.495 ppm 28.7 to 0.05 mg/L (pH 5-9)	USEPA 1997 Cleveland et al. 2002

Methyl eugenol is a colorless liquid with the odor of cloves. The CAS # is 93-15-2. The chemical structure of methyl eugenol is shown in Figure 2-2. Water solubility is less than 0.1 g/100mL at 19°C. Vapor pressure is 0.01 mm Hg at 20°C (USEPA 2004).

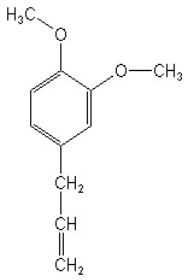

Figure 2-2 Chemical Structure of Methyl Eugenol

2.3 Environmental Fate

The environmental fate describes the processes by which spinosad 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.

Spinosad persistence in the environment is variable in terrestrial and aquatic systems (Table 2-2) (USEPA 1998). Spinosad is not sensitive to hydrolysis but breaks down rapidly in water in the presence of light with reported photolytic half-lives of less than 1 day. The rapid photolytic breakdown of spinosad in laboratory studies has also been confirmed in microcosm studies (Cleveland et al. 2002). Solubility of spinosad in water is pH dependent and is dependent on the structurally similar active ingredients. Solubility for spinosyn A ranges from 290 to 16 mg/L with increasing pH, while the solubility for spinosyn D is much less but still pH-dependent with values ranging from 28.7 to 0.05 mg/L for pH values between five and nine (Cleveland et al. 2002).

Table 2-2. Reported Half-lives for Spinosad in Soil and Water.

Environmental Fate Parameter	**Reported Half-life**
Hydrolysis (Spinosyn A/D)	No degradation @ pH 5 and 7, pH 9 (200/259 days)
Aqueous Photolysis (Spinosyn A/D)	0.93/0.82 days @ pH 7
Soil Photolysis (Spinosyn A/D)	82/44 days
Aerobic Soil Metabolism (Spinosyn A/D)	9.0–17.3/14.5 days
Anaerobic Aquatic Metabolism (Spinosyn A/D)	161/ 205 days
Terrestrial Field Dissipation	0.3 to 0.5 days for Spinosyn A

Degradation of spinosyn A and D in soil is rapid under aerobic conditions suggesting spinosad is susceptible to microbial degradation (EPA 1998a, Hale and Portwood 1996). Spinosad also degrades quickly on plant surfaces with reported half-lives ranging from 2.0 to 11.7 days (CDPR 2002, Sharma et al. 2008).

Spinosad is not considered mobile based on the available soil adsorption (Koc) studies that have been conducted on a range of soil types. Values range from 884 to 145,350, with the lowest value occurring in a loamy sand with 1.1 percent organic matter and a cation exchange capacity

(cec) of 1.9, while the highest value is for a silt loam soil with 0.4 percent organic matter and a cec of 12.0 (CDPR 2002).

Spinosad is not considered to be volatile based on the vapor pressure for both active ingredients, with values of 2.4×10^{-10} mm Hg for spinosyn A and 1.6×10^{-10} mm Hg for spinosyn D (Cleveland et al., 2002). Chemicals with vapor pressure values less that 1×10^{-6} are considered nonvolatile (CDPR 2002).

Methyl eugenol is a volatile compound. In the atmosphere, methyl eugenol will be degraded by reaction with photochemically-produced hydroxyl radicals. The half-life for this reaction in air is estimated to be 5 hours (Toxnet 2013). Based upon an estimated Koc of 140, methyl eugenol released to soil is expected to have high mobility, and methyl eugenol released to water is expected to adsorb moderately to suspended solids and sediment. Based upon an estimated Henry's Law constant of 5.6×10^{-6} atm-cu m/mole, methyl eugenol in moist soil surface and water surface is expected to volatilize. Dissipation half-lives of 6 and 16 hours (at 32 and 22 deg C, respectively) in soil and 6 and 34 hours (at 32 and 22 deg C, respectively) in water have been reported. Methyl eugenol in water is not expected to undergo hydrolysis in the environment due to the lack of hydrolysable functional groups (Toxnet 2013). Modelling predicted half-lives of methyl eugenol in soil, water, and sediment were 8 days, 8 days, and 32 days, respectively. These predicted half-lives suggested that methyl eugenol is expected to reside mainly in the environmental compartment to which it is released (Environment Canada 2010).

The active ingredients in STATIC™ Spinosad ME are applied within a waxy formulation carrier, which serves to impart increased residual and rainfastness to the active ingredient and methyl eugenol lure. Therefore, the degradation rates of the active ingredient are lower.

2.4 Hazard Identification

Spinosad has low acute toxicity and is classified by USEPA as Toxicity Category III (slightly toxic with "caution" warning on label) for acute oral and dermal toxicity and Toxicity Category IV (Not acutely toxic with no warning on label) for acute inhalation toxicity, primary eye irritation, and primary skin irritation (USEPA 2005). The rat oral median lethal dose (LD_{50}) is 3,738 mg/kg for males and >5,000 mg/kg for females, whereas the mouse oral LD_{50} is >5,000 mg/kg. The rabbit dermal LD_{50} is >2,000 mg/kg and the rat inhalation median lethal concentration (LC_{50}) is >5.18 mg/l air (USEPA 1998).

In subchronic toxicity studes the primary effects in mouse were increased vacuolation of cells in the lymphoid organs, liver, kidney, stomach, female reproductive tract, and epididymis, and less severely in the heart, lung, pancreas, adrenal cortex, bone marrow, tongue, pituitary gland, and anemia. Thyroid follicle epithelial cell vacuolation, anemia, multifocal hepatocellular granuloma, cardiomyopathy and spleenic histiocytosis were observed in rats. Microscopic changes in a variety of tissues, anemia, and possible liver damage were observed in dogs (USEPA 2005). Spinosad was evaluated in 13-week dietary studies and showed No Observable Effect Levels (NOELs) of 4.9 mg/kg/day in dogs, 6 mg/kg/day in mice, and 8.6 mg/kg/day in rats. No dermal irritation or systemic toxicity occurred in a 21-day repeated dose dermal toxicity study in rabbits at 1,000 mg/kg/day (USEPA 1998). It is not a dermal sensitizer based on a lack

of toxicity observed at the limit dose in a 21-day dermal toxicity study using rabbits (USEPA 2005).

Chronic toxicity studies in the dog and rat report NOELs of 2.68 and 2.72 mg/kg/day, respectively for male and female dogs, and 2.4 and 3.0 mg/kg/day, respectively for male and female rats.

Spinosad is not a neurotoxic agent in acute, subchronic, or chronic toxicity studies. No neurotoxic effects were observed at the limit dose in an acute neurotoxicity study in rats and at doses up to 42.7 mg/kg/day in a subchronic neurotoxicity study. In a chronic feeding study in dogs, increases in serum alanine aminotransferase, aspartate aminotransferase, and triglycerides levels, and the presence of tissue abnormalities, including vacuolated cell aggregations, arteritis, and glandular cell vacuolation (parathyroid) were observed. In a chronic oral toxicity study in rats, vacuolation of thyroid follicular cells, increased absolute, and relative thyroid weights were observed. In mice, rats, and dogs, other organs including liver, kidney, spleen, heart, thyroid, and bone marrow (anemia) appeared to be the target organs (USEPA 2005).

No developmental effects were observed in the rat and rabbit developmental toxicity studies. In a 2-generation reproduction study in rats, decreased litter size and survival was observed in the presence of maternal toxicity (deaths) at the highest dose tested. However, the maternal and offspring toxicity (deaths) indicated no evidence of increased susceptibility in this study (USEPA 2005).

There were no major differences in the bioavailability, routes or rates of excretion, or metabolism following a single low oral dose, single high oral dose, or repeated oral doses in rats. Most of the dose (approximately 70-80%) was absorbed. Approximately 20% of the dose was eliminated in the feces which was the major route of excretion. The excreted metabolites were glutathione conjugates of the parent and O-demethylated Factor A. Metabolites in the tissues were the N-and O-demethylated Factor A. With rapid biliary excretion, metabolites in the bile were the glutathione conjugates of parent and N-and O-demethylated forms of Factor D (USEPA 2005).

Carcinogenicity/Mutagenicity:

Carcinogenic toxicity studies show spinosad is not likely to be carcinogenic (USEPA 1998, Yano et al. 2002, Stebbins et al. 2002, USEPA 2005). It is also negative for mutagenicity in various mutagenicity assays.

Endocrine disruption:

A literature search regarding available spinosad toxicity studies show that there was no estrogen or thyroid mediated toxicity (USEPA 2005).

Spinosad is not among the group of 58 pesticide active ingredients on the initial list to be screened under the EPA Endocrine Disruptor Screening Program. This program determines whether certain substances may have an effect in humans or wildlife similar to an effect

produced by a "naturally occurring estrogen, or other such endocrine effects as the Administrator may designate". Spinosad is not on the USEPA Draft Second Endocrine Disruptor Screening Program (EDSP) List of Chemicals for Tier 1 Screening (USEPA 2010). USEPA considers that the compounds on the list are candidates (at least for screening purposes) under EDSP testing based only on their pesticide registration status and/or because such substances may occur in sources of drinking water to which a substantial population may be exposed (USEPA 2013b).

Other ingredients:

Methy eugenol is another ingredient in the formulation used as a chemical attractant for fruit flies. Methyl eugenol is a naturally occurring constituent found in a number of plants such as nutmeg, pimento, lemongrass, tarragon, basil, star anise and fennel (European Commission 2001).

Methyl eugenol is considered moderately toxic to mammals with median lethal oral doses of 810 to 1,560 mg/kg for rats and 540 mg/kg for mice. The undiluted chemical (98% purity) is not considered an eye or a skin irritant (NTP 2000). Methyl eugenol is considered practically nontoxic in dermal or inhalation acute exposures (Beroza et al. 1975). Longer term studies using methyl eugenol have also been conducted using rats and mice. In a 14-week study, a dose of 0, 10, 30, 100, 300 or 1000 mg methyl eugenol/kg body weight in 0.5% aqueous methylcellulose were administered to groups of 10 males and 10 females per sex per species by gavage (5 days per week) (Abdo et al. 2001). Methyl eugenol administration to rats induced erythrocyte microcytosis, thrombocytosis, hypoproteinemia, and hypoalbuminemia. It caused an increase in serum alanine aminotransferase and sorbitol dehydrogenase activities and bile acid concentration. Methyl eugenol also caused an increase in the incidence of hepatocyte cytologic alteration, cytomegaly, Kupffer cell pigmentation, mixed foci of cellular alteration and bile duct hyperplasia of the liver and atrophy and chronic inflammation of the mucosa of the glandular stomach. In mice, methyl eugenol caused an increase in the incidence of cytologic alteration, necrosis, bile duct hyperplasia and subacute inflammation of the liver and atrophy, degeneration, necrosis, edema, mitotic alteration, and cystic glands of the fundic region of the glandular stomach. The NOEL of methyl eugenol for both species was estimated at 10 mg/kg (NTP 2013). In long-term exposures the National Toxicology Program (NTP) conducted 2-year studies in rats and mice and concluded that there was clear evidence of carcinogenic activity in male and female F344/N rats, based on an increase incidence of liver neoplasms and neuroendocrine tumors of the glandular stomach in male and female rats, and increased incidence of kidney neoplasms, malignant fibroma and fibroma or fibrosarcoma (combined) in male rats (NTP 2000, 2013). Dose rates in both studies ranged from 37 mg/kg to 150 mg/kg with the dose-related effects varying based on the endpoint and a NOEL not reported for either test species. Methyl eugenol is not considered to be mutagenic and in metabolism studies has been shown to be rapidly eliminated and excreted from human blood serum (NTP 2013, Schecter et al. 2004).

The reported effects of methyl eugenol are at doses above those expected to occur in human populations and is reflected in the USEPA's Tolerance Reassessment Eligibility Document for methyl eugenol that concluded *"...there is a reasonable certainty that no harm to any population or subgroup will result from the dietary and water exposure to methyl eugenol from uses specified in the existing exemption for the requirements for tolerance for methyl eugenol under*

40 CFR §180.1067." (USEPA 2006). In addition the Food and Drug Admnistration (FDA) classifies methyl eugenol as a "Generally Recognized as Safe (GRAS)" compound suggesting a low hazard to human health.

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 toxicities.

USEPA established a chronic oral reference dose (RfD) of 0.0268 mg/kg/day for spinosad based on chronic toxicity studies with the dog and rat. This RfD has incorporated a 100-fold safety factor to the NOELs (see Section 2.4) found in the chronic dog study to include animal to human extrapolation (an uncertainty factor of 10) and sensitive subgroups with a population (an uncertainty factor of 10) (USEPA 1998). For occupational exposure, the RfD is 0.27 mg/kg/day because the uncertainty factor of 10 for protection of sensitive subgroups such as infants or children is not applicable. The RfD for occupational exposure of 0.27 mg/kg/day is used for this human health risk assessment.

3.2 Ecological Dose-Response Assessment

3.2.1 Wild Mammal Toxicity

The acute and chronic toxicity of spinosad to wild mammals is expected to be low from oral, dermal and inhalation exposures based on the available data summarized above in the hazard identification section of this risk assessment. Using the lowest reported acute LD_{50} value and the lowest subchronic rat NOEL, adjusted LD_{50} and NOEL values were calculated for different size mammals (Table 3-1). The ranges of different body weights and consumption rates were selected to represent mammals, such as the shrew that consumes a large percentage of their body weight and may receive higher exposure, as well as larger mammals (1 kg) that may consume less when compared to the standard laboratory rat, which is used in several of the mammalian toxicity studies. The lowest subchronic value was selected due to the short environmental half-life of spinosad. Effects from daily exposure over a 13-week period are not expected but provide a conservative estimate of effects. These values are also lower than any of the developmental and reproductive NOEL values that have been determined in previous studies.

Table 3-1. Adjusted LD_{50} and NOEL Values for Select Mammals.

Mammalian Class	Body Weight (g)	% Body Weight Consumed	Adjusted LD_{50}	Adjusted NOEL
Herbivores/ Insectivores	15	95	8433.08	16.48
	35	66	6823.26	13.34
	1,000	15	2951.27	5.77
Granivores	15	21	8433.08	16.48
	35	15	6823.26	13.34
	1,000	3	2951.27	5.77

3.2.2 Avian and Reptile Toxicity

Spinosad acute and chronic toxicity to birds is low for both surrogate species that have been tested (Table 3-2). Acute LD_{50} and LC_{50} for the mallard and bobwhite quail are greater than the highest concentration tested, 1,333 mg/kg and 5,156 parts per million (ppm), respectively (EPA, 2010). Chronic toxicity is also low with reproduction NOEC values of 500 ppm for the mallard and 550 ppm for the bobwhite quail in 20-week exposure studies.

Table 3-2. Acute and Chronic Avian Toxicity of Spinosad.

Test Species/ Duration	LD_{50}/LC_{50} (mg/kg)	NOEL/LOEL (mg/kg)
Bobwhite quail, *Colinus virginianus* LD_{50}	>1333	500/NR
Bobwhite quail LC_{50}	>5156	656/NR
Bobwhite quail chronic reproduction	NR	550/1100
Mallard, *Anas platyrhynchos* LD_{50}	>1333	1333/NR
Mallard LC_{50}	>5156	302/NR
Mallard chronic reproduction	NR	500/1100

NR = Not reported

The lowest acute NOEL value (500 mg/kg) was used to estimate an adjusted sublethal toxicity value for birds of different sizes and feeding rates (table 3-3). Based on the adjusted body weight for different avian size classes and their percentage of body weight consumed, adjusted NOEL values ranged from approximately 360 to 648 mg/kg.

Table 3-3. Adjusted Acute Toxicity Values for Different Sized Birds.

Avian Class	Body Weight (g)	% Body Weight Consumed	Adjusted NOEL
Small	20	114	360.21
Mid	100	65	458.57
Large	1000	29	647.75

No reptile toxicity data appears to be available for spinosad. USEPA/OPP uses the effects data for birds to represent sensitivity to reptiles. There is uncertainty in this assumption; however, based on the low toxicity of spinosad to birds and mammals, as well as aquatic vertebrates, toxicity to reptiles would also be expected to be low.

3.2.3 Terrestrial Invertebrate Toxicity

Toxicity to terrestrial invertebrates is variable based on the available toxicity data for pests, pollinators, and biocontrol agents. Honey bees appear to be one of the more sensitive terrestrial invertebrates to spinosad, with 48-hour contact LD_{50} values ranging from 0.0029 to 0.078 µg ai/bee and a reported NOEC of 0.0016 µg ai/bee (0.016 µg/g) (Mayes et al. 2003). Toxicity to honey bees is similar to other native bees with reported contact LD_{50} values of 0.058, 0.065, and 0.078 µg ai/bee for the alfalfa leafcutter bee (*Megachile rotundata*), alkali bee (*Nomia melanderi*) and honey bee, respectively (Mayer et al., 2001). Contact toxicity to spinosad decreases rapidly after applications are allowed to dry. Laboratory, greenhouse, and field studies have demonstrated that spinosad is nontoxic to bees 3 hours after application (Mayes et al., 2003). Studies using honey bees and bumblebees exposed to spinosad residues on alfalfa, strawberries, almonds, citrus, and kiwifruit have documented a lack of impacts to pollinators when applications are made when bees are not active, and after residues have weathered. Toxicity to other nontarget insects ranges from 3.3 to greater than 200 mg/L based on reported LC_{50} values (Thompson et al. 2000, Williams et al. 2003, Penagos et al. 2005, Miles and Eelen 2006, Semiz et al. 2006). Within Lepidoptera, sensitivity can vary with effective treatment rates ranging from 25 to 360 g/ha (Thompson et al. 2000). Lepidoptera appear to be less sensitive to spinosad compared to pollinators, such as honey bees and bumblebees. For example, contact toxicity of fourth instar *Spodoptera littoralis* larvae to spinosad is reported as 4.74 µg/g, which is lower than the 0.029 µg/g reported for the honey bee (Pineda et al. 2006). Dietary spinosad LC_{50} values for *S. littoralis* range from 0.5 to 2.98 ppm.
Based on field-collected data, there were no effects on abundance and diversity of Lepidoptera, Coleoptera, or Hymenoptera when sampled using malaise traps 2 and 6 days after spinosad treatment for emerald ash borer (USDA APHIS 2007). Aerial broadcast applications were made to several plots ranging in size from 8 to 20 acres at a rate (0.23 lb ai/ac) which is greater than two orders of magnitude above the use rate proposed in the fruit fly program. Non-target terrestrial invertebrate impacts have also been evaluated using this specific combination of spinosad and the attractant methyl eugenol. Methyl eugenol is a naturally occurring chemical produced in over 450 plant species with varied effects on terrestrial invertebrates (Tan and Nishida 2012). Stark et al. (2004) demonstrated that contact toxicity of spinosad to two parasitoids only occurred at levels well above those that would be encountered in any field setting.

3.2.4 Terrestrial Plant Toxicity

No terrestrial phytotoxicity has been noted using spinosad at rates up to 0.18 lb ai/ac (EPA 1998a).

3.2.5 Aquatic Toxicity

Spinosad has moderate toxicity to fish based on the available toxicity data, with acute toxicity values ranging from 4.99 to 30 mg/L in 96-hour exposures (Table 3-4).

Table 3-4. Spinosad Aquatic Toxicity Values for Aquatic Vertebrates.

Test Species/Duration	**LC_{50}/EC_{50} (mg/L)**	**NOEC/LOEC (mg/L)**
Acute Tests		
96-hour LC_{50} Carp *Cyprinus carpio*	4.99	NR
96-hour LC_{50} Bluegill Sunfish *Lepomis macrochirus*	5.9	2.10/NR
96-hour LC_{50} Rainbow Trout *Oncorynchus mykiss*	30	5.2/NR
96-hour LC_{50} Sheepshead Minnow *Cyprinodon variegates*	7.87	1.8/NR
Subchronic Tests		
Rainbow Trout ELS*	NR	0.498/0.962
Rainbow Trout 21-d	NR	1.2/2.1
Sheepshead 35-d ELS	NR	1.15/2.38

*ELS = Early life stage study; NR = Not reported

A literature review revealed no apparent toxicity data for spinosad on amphibians. EPA–OPP uses fish toxicity data to represent the sensitivity of amphibians which provides uncertainty due to potential differences in sensitivities, and differences in exposure pathways between fish and adult amphibians. However, due to the lack of amphibian-related data for spinosad, fish effects data will be used as a surrogate and discussed in relation to risk in the below aquatic risk characterization section.

Based on the available aquatic toxicity profile, spinosad has variable toxicity to aquatic invertebrates (Table 3-5) (EPA 1998a, Stark and Banks 2001, Cleveland et al. 2001). Longer term studies show that under continuous exposure for 21 days, spinosad has a greater effect on the freshwater cladoceran, *Daphnia magna*. The same study using pulse doses within a short period of time demonstrates the rapid breakdown of spinosad with an approximate tenfold decrease in toxicity. Stark and Vargas (2003) demonstrated demographic effects to *D. pulex* populations exposed to formulated spinosad at 8 µg/L and greater in 60- to 70-day exposures. Test chambers were renewed every other day for the duration of the study. In a long-term sediment study, the midge *Chironomus riparius* was shown to have lower chronic sensitivity when compared to *D. magna* tested under continuous exposure conditions.

Table 3-5. Spinosad Aquatic Toxicity Values for Aquatic Invertebrates.

Test Duration/Species	LC_{50}/EC_{50} (mg/L)	NOEC/LOEC (mg/L)
Acute Tests		
48-hour EC_{50} *Daphnia magna*	14.0	0.45/NR
96-hour LC_{50} Grass Shrimp	>9.76	1.66/NR
96-hour LC_{50} Eastern Oyster	0.30	0.14/NR
24-hour LC_{50} *Aedes aegypti*	0.025	NR
24-hour LC_{50} *A. aegypti* (4^{th} instar)	0.160	NR
72-hour LC_{50} *A. aegypti* (Adults)	0.460	NR
Chronic Tests		
21-day LC_{50} *D. magna* (continuous)	>0.006	NR
21-day LC_{50} *D. magna* (5-d pulse)	>0.057	NR
28-day Mysid Life Cycle	NR	0.084/0.173
25-day LC_{50} *Chironomus riparius*	> 0.003	1.6
21-day *D. magna* (continuous)	NR	0.617/1.2 (µg/L)
21-day *D. magna* (5-d pulse)	NR	1.6/3.2 (µg/L)
25-day *C. riparius*	NR	84.2/173 (µg/L)

NR = Not reported

Mosquito species, such as *Culex pipiens, Aedes aegypti*, and *A. albimanus* appear to be the most sensitive aquatic invertebate taxa to spinosad, while the cladoceran *D. magna* was the least sensitive with a 48-hour EC_{50} of 14 mg/L (EPA 1998a, Bond et al. 2004). Mosquito sensitivity was comparable between technical and formulated spinosad based on the available data using other spinosad formulations (Bond et al. 2004, Cetin et al. 2005, Stevens et al. 2005, Ayesa et al. 2006).

Toxicity to aquatic plants, such as diatoms and algae, range from 0.107 mg/L for the freshwater diatom, *Navicula pelliculosa,* to greater than 105.5 mg/L for green algae based on 5-day exposures (EPA 2010). Toxicity to aquatic macrophytes is based on a 14-day EC_{50} value for duckweed, *Lemna gibba*, which was reported as 10.6 mg/L.

3.2.6 Metabolite and Formulation Toxicity

Available acute and chronic aquatic toxicity data for metabolites of spinosyn A and D demonstrate that metabolites are less toxic than the parent material (Table 3-6) (USEPA 2013c). The spinosyn A metabolite has a sublethal toxicity value that is more than 160 times below the reported spinosad NOEC for *D. magna*. The same is true when comparing chronic toxicity values for *D. magna* between the parent and metabolite. Based on NOEC values from the 21-day studies, the spinosyn A metabolite is more than 15,000 times less toxic than the parent. Similar reductions in toxicity are also observed when comparing spinosad aquatic invertebrate toxicity to the primary metabolite for spinosyn D.

Table 3-6. Spinosyn Metabolite Aquatic Toxicity Values for Aquatic Biota.

Test Duration/ Species	LC_{50}/EC_{50} (mg/L)	NOEC/LOEC (mg/L)
Spinosyn A metabolite		
48-hour EC_{50} *D. magna*	> 197.0	74.7/NR
21-day *D. magna* reproduction	NR	9.32/>9.32
28-day *C. riparius*	>0.073	0.073/NR
96-hour *Navicula pelliculosa*	31.0	17.2/NR
Spinosyn D metabolite		
48-hour EC_{50} *D. magna*	66.8	46.4/NR
21-day *D. magna* reproduction	NR	4.85/9.32
28-day *C. riparius*	>0.039	0.039
96-hour *N. pelliculosa*	19.0	14.2/NR
120-hour *N. pelliculosa*	0.22	0.17/NR

NR = Not reported

No aquatic ecological effects data is available for the proposed formulation however available data on other formulations of spinosad, and the other primary product in the formulation, methyl eugenol, suggest toxicity will occur primarily through exposure to spinosad. Methyl eugenol comprises 51% of the proposed formulation. Reported methyl eugenol 96-hour acute aquatic toxicity values range from 6.9 mg/L for the rainbow trout and 8.1 mg/L for the bluegill sunfish (Beroza et al. 1975). These values are in the same range of acute toxicity values for fish and spinosad however the methyl eugenol toxicity values exceed the solubility for methyl eugenol and therefore would not occur in aquatic systems. Available aquatic invertebrate data is limited however median lethality values for various mosquito species exceed 50 mg/L which is well above the solubility limit for methyl eugenol (Perumalsamy et al. 2010). Toxicity to terrestrial wildlife is expected to be similar between the formulation and technical active ingredient based on the previously discussed acute mammalian formulation data and the technical active ingredient.

4.0 EXPOSURE ASSESSMENT

4.1 Human Health Exposure Assessment

Exposure assessment estimates the potential exposure of humans to spinosad. The exposure assessment begins with the use and application method of STATIC™ Spinosad ME. A complete exposure pathway for spinosad includes (1) a release from a spinosad source, (2) an exposure point where contact can occur, and (3) an exposure route such as ingestion, inhalation, or dermal contact by which contact can occur (USEPA 1989). Exposures for the identified human populations are evaluated for each identified exposure pathway.

4.1.1 Potentially Exposed Human Populations and Complete Exposure Pathways

The STATIC™ Spinosad ME formulation is used as a bait (small dollops or large droplets) and hand applied using a spatula or other spreading implement, or pneumatic meter-jet capable of delivering large droplets. STATIC™ Spinosad ME is expected to be applied to sites higher up on telephone poles, light poles, fences, other inanimate objects, non-crop tree trunks or limbs, non-edible foliage where it is not readily accessible to the general public. Therefore, workers (i.e. handlers) in the program are the most likely subgroup that could be exposed to spinosad. The potential exposure to workers to spinosad is from mixing (thorough stirring and mixing of the formulation is required prior to use although the formulation is ready-to-use) and application activities. Under normal applications, the potential for handlers to be exposed to spinosad is minimal from mixing and spot application with adherence to labeled requirements for personal protective equipment (PPE) (long-sleeved shirt and long pants, shoes and socks, and chemical-resistant gloves). Under the accidental event when PPEs do not function properly, the complete exposure pathway for these workers includes dermal contact and is further evaluated in Section 6. Inhalation route is not complete for spinosad because spinosad is not volatile, and exposure from the inhalation route is limited for methyl eugenol during stirring and mixing of the waxy formulation. Incidental ingestion route is not complete under the spot application method.

The general public such as residents is not identified as a potentially exposed human population because their exposure to spinosad in STATIC™ Spinosad ME bait formulation is extremely unlikely when the locations of the baits are not readily accessible to the general public.

A complete exposure pathway is not identified for dietary plant consumption or dermal contact to plants because the STATIC™ Spinosad ME bait is not applied to plants that would be harvested for human consumption. In addition, spinosad degrades quickly on plant surfaces (see Section 2.3).

A complete exposure pathway is not identified for the groundwater medium or surface water medium based on the specific spot application method required by the label. Surface runoff via rain fall may occur, however, the amount of spinosad from this bait formulation releasing to soil is minimal based on the proposed low application rates. In addition this particular formulation of spinosad within a waxy carrier is rain fast and would not be expected to be removed from the site of application until after significant weathering and degradation occurs reducing the amount of spinosad available for runoff to receiving water that could serve as a drinking water source.

4.1.2 Exposure Evaluation

This section quantitatively evaluates the worker accidental exposures from dermal contact pathway while mixing, loading, and applying the spinosad baits. Under the accidental exposure scenario, it assumes that chemical-resistant gloves are broken.

Chemical-specific data to assess potential exposure to occupational pesticide handlers were not available. The estimates of exposure to pesticide handlers are based on surrogate study data available in the Pesticide Handlers Exposure Database (PHED) (USEPA 2013d). The mixer/loader/applicator, mechanically-pressurized handgun sprayer in orchards, vineyards, specialty agricultural crops, rights-of-way, nurseries, landscaping (non-turf),

industrial/commercial areas, aquatic areas for drench/soil directed applications and all formulations, except wettable powders exposure scenario with single layer (long-sleeve shirt, long pants, shoes plus socks) and no gloves is the closest scenario to represent the mixing, loading and spot application of the formulation and is used for the dermal exposure evaluation. The unit exposure for the surrogate scenario is 1300 µg/lb ai. Application rates range from 0.0045 to 0.009 lb ai/acre. The following equations are used to estimate the exposure dose of dermal contact for workers:

Exposure Dose = Daily Dose Rate/Body Weight
Daily Dose Rate = Unit Exposure (mg/lb ai) x Application Rate (lb ai/acre) x Area Treated (acre/day)

The exposure doses were estimated for the application rates and summarized in Appendix A.

4.2 Ecological Exposure Assessment

4.2.1 Terrestrial Exposure Pathway Evaluation

The potential for exposure of nontarget terrestrial vertebrates to the proposed formulation of spinosad is minimal through either the dermal, inhalation or dietary routes. The lack of dietary exposure is based on the method of application which will not include objects that would be consumed by nontarget vertebrates (ex. light poles, tree trunks). Dermal exposure would also be low and would only occur when a nontarget vertebrate would come into contact with the material while moving over an area on a pole or tree where an application was made. Inhalation exposure would also be low due to the method of application and low volatility of spinosad. There is the potential for some inhalation exposure to methyl eugenol due to its volatility however methyl eugenol is a naturally occurring phenylpropanoid compound that is released when plants are damaged and its use in this program would not be expected to result in exposures to terrestrial vertebrates beyond ambient levels.

4.2.2 Aquatic Exposure Pathway Evaluation

Exposure to aquatic biota from the proposed use of spinosad is expected to result in negligible residues based on the use pattern and low application rates. Applications are hand applied to specific objects such as light and telephones poles, tree limbs as either large dollops are very large droplets that would not be susceptible to drift. A possible scenario of aquatic exposure could occur where a dollop or large droplet becomes dislodged from the site of application after it has weathered and washed into a receiving stream. This scenario would result in negligible residues based on conservative estimates of spinosad transport into water bodies. Assuming the maximum application rate for spinosad (0.009 lb ai/ac) is discharged into a water body such as a wetland that is one acre in size and six inches deep would result in a spinosad reside of 3.3 µg/L. This very conservative assumption assumes all material applied in one acre is available for transport and that no degradation would occur. Residues into other larger bodies of water or those where water is running would result in substantially lower residues due to the dilution in those types of water bodies.

5.0 RISK CHARACTERIZATION

5.1 Human Health

Risks associated with adverse human health and fish and wildlife are characterized quantitatively and qualitatively in this section. Under the proposed use, STATIC™ Spinosad ME baits for spot application to eradicate fruit flies poses minimal risk to human health due to limited exposure for applicators using appropriate PPE and the low acute toxicity of spinosad to mammals. Accidental risk (hazard quotient) was estimated by dividing the exposure doses with the toxicity value (RfD) for the handler dermal contact exposure scenario. The estimated risk for labeled application rates is low with hazard quotients three to four orders of magnitude below one indicating risk from accidental spinosad exposure is minimal (Appendix A).

The general public is not a concern because STATIC™ Spinosad ME will be applied to sites on telephone poles, light poles, fences, other inanimate objects, non-crop tree trunks or limbs and non-edible foliage where the material is not readily accessible.

5.2 Ecological

Risks to fish and wildlife are anticipated to be minimal based on the favorable toxicity profile for spinosad, its environmental fate and the proposed use pattern in the fruit fly program. Direct risk to terrestrial vertebrates from ingestion of the bait is extremely low since applications aren't directed to food items such as seeds, fruits and insects that would contain spinosad residues. In cases where terrestrial vertebrates would consume the bait, they would have to consume many times their body weight to receive a dose that could result in any effects which is highly unlikely. Risk to food items or shelter required by terrestrial vertebrates would also not be anticipated due to the method of application, the selective nature of the bait to certain invertebrates and lack of risk to terrestrial or aquatic plants. There is some risk to certain terrestrial invertebrates that are attracted to the bait due to the presence of methyl eugenol, and could receive a lethal dose of spinosad, however, based on the selective nature of methyl eugenol and spinosad as well as field collected data the impacts would be localized and transient and not anticipated to result in population level effects to sensitive taxa including beneficial arthropods.

Aquatic vertebrates and invertebrates are also at low risk from the proposed spinosad applications. The method of application eliminates the potential for off-site drift and runoff and would only occur in cases where baits become weathered and fall from where they were applied, and then carried to aquatic areas. A comparison of the aquatic residue from the wetland habitat that was estimated in the exposure analysis to the available fish effects data shows that the exposure concentration is at least two orders of magnitude below the acute and chronic effects data for fish suggesting minimal risk (Figure 5-1). Acute risk to aquatic invertebrates is also low with the range of sensitivities well above the estimated residue in a wetland habitat. The 25-day chronic study with the midge has an effect level below the aquatic residue value while the remaining chronic aquatic invertebrate values are well above the instantaneous residue value suggesting minimal chronic risk to most aquatic invertebrates. Exceeding the chronic exposure value in the midge study does not imply risk to this group of organisms due to the conservative assumptions that were made to calculate an exposure value. Not all of the material would be

expected to become dislodged from the point of application at the same time and simultaneously released into a water body. In addition any exposure that would occur would not be continuous over a 25 day period as was done in this study due to spinosad degradation/partitioning in aquatic systems. Degradation would result in a further decrease in risk since the metabolites are less toxic than the parent.

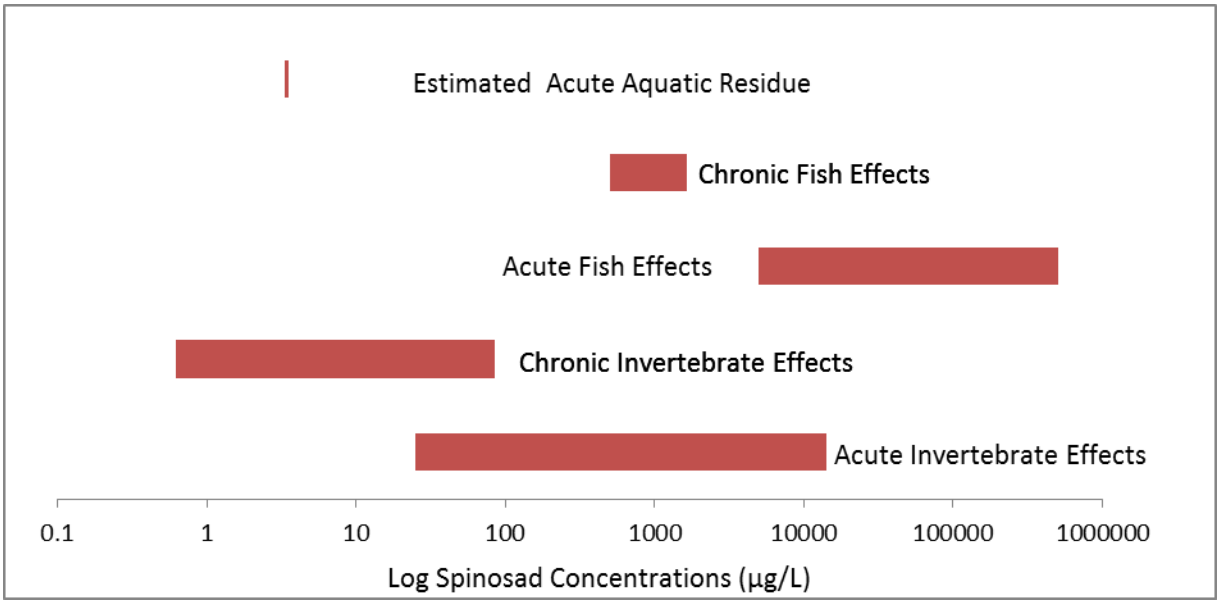

Figure 5-1. Aquatic risk characterization for spinosad.

The lack of risk to both aquatic vertebrates and invertebrates ensures that the direct risk to fish is minimal and that their prey base would also be at low risk from the proposed applications of spinosad.

6.0 UNCERTAINTIES/CUMULATIVE EFFECTS

Uncertainties and cumulative impacts associated with the risk evaluation are qualitatively discussed in this section.

Accidental human exposure to spinosad in baits during mixing, loading, and applying may occur to handlers when label required PPEs do not function properly. The RTU formulation serves to minimize worker exposure as no mixing is required. Surrogate study data available in the PHED were used for the accidental exposure rate since chemical-specific data to assess potential exposure to occupational pesticide handlers were not available. The closest surrogate study to the spot application of STATIC™ spinosad ME is the mixer/loader/applicator, mechanical-pressurized handgun sprayer scenario for drench/soil directed applications and all formulations, except the wettable powder exposure scenario with single layer and no gloves. However, this scenario is more conservative than the spot application scenario for the proposed formulation

because more exposure will occur in the mechanical-pressurized handgun sprayer scenario than for placement of a single spot of pesticide.

Uncertainties in the ecological risk assessment sections of this document are similar to those for other pesticides and chemicals. For example the applicability of surrogate laboratory toxicity studies to natural ecosystems is an area of uncertainty in ecological risk assessment methodology. The approach in this assessment was to make assumptions regarding exposure that were very conservative and designed to account for some of the uncertainty common with screening level ecological risk assessments that rely on standardized toxicity data. Other areas of potential uncertainty in these types of assessments are with effects data for the metabolites and formulated material, however data was available to demonstrate that common metabolites of spinosad are less toxic than the parent material.

Another area of uncertainty in this risk assessment is related to the potential for cumulative effects. The potential for cumulative effects can occur through various exposure pathways such as 1) repeated exposure to spinosad; 2) co-exposures to other pesticides within the program with respect to their toxicity; 3) exposures to other chemicals impacting the toxicity of spinosad; and 4) exposures to spinosad from other sources.

Spinosad has other labeled food and non-food uses and is currently used in the APHIS Fruit Fly Eradication Program as well as other APHIS programs such as the European Grapevine Moth. Cumulatively there would be an increase in spinosad use in relation to other APHIS and non-APHIS spinosad uses however the effects to human health and the environment are expected to be incrementally negligible, and in cases where it is used as a naled replacement, would be beneficial. From a human health perspective repeated exposure to workers would not be expected to result in significant cumulative effects due to the use of PPE and the very low risk that was determined in this risk assessment. Cumulative effects to the general population are also not anticipated since the likelihood of exposure is very low in this program since applications are made to non-food items and there is a very low likelihood of any residues in drinking water. A lack of cumulative effects would also be anticipated as it relates to other chemicals since the risk to workers and the general population is very low from the proposed use of spinosad in the program.

Neither spinosad nor methyl eugenol are among the five common mechanism groups of pesticides (Organophosphates, N-methyl Carbamates, Triazines, Chloroacetanilides, and Pyrethrins/Pyrethroids). USEPA defines that common mechanism of toxicity pertains to two or more pesticide chemicals or other substances that cause a common toxic effect(s) by the same, or essentially the same, sequence of major biochemical events (USEPA 2013e)

Cumulative impacts to aquatic and terrestrial nontarget organisms are expected to be negligible. The proposed use pattern for this formulation is not expected to result in risk to nontarget terrestrial vertebrates from direct effects or through impacts to available prey or habitat. The lack of significant ecological risk from spinosad use in this program would suggest that significant cumulative effects to nontarget organisms from other stressors would be incrementally minor. The selective nature of the use of spinosad in the fruit fly program also

ensures that any cumulative impacts to beneficial insects from the use of spinosad in this program would be minor and pose less risk than the use of naled in the same formulation type.

Water quality data in the United States, including areas where fruit fly program activities may occur, show pesticide mixtures to be a common occurrence in surface water with varying impacts to aquatic organisms (USGS 2006). Some of these bodies of water may be listed impaired under Section 303(d) of the Clean Water Act due to pesticides, or some another abiotic or biotic stressor. The impact to water bodies from any spinosad residues that could occur from use in the Fruit Fly Eradication Program is expected to be incrementally negligible to water bodies that may already be impacted by other contaminants. The waxy materials in STATIC™ Spinosad ME increase rainfastness of the bait and reduce runoff. The proposed method of application mitigates any impacts from drift and makes runoff unlikely so that any residues that could potentially occur in water would not be expected to result in impacts to aquatic biota. The impacts of potential mixtures at any concentration are an area of uncertainty due to the large number of potential types of chemical mixtures that could occur, and the spatial and temporal variability in their occurrence. Spinosad has been shown to have greater than additive effects to aquatic invertebrates such as mosquitos however these occur at doses well above those that would occur in this program (Darriet and Corbel, 2006). The low potential for risk to aquatic biota from spinosad applications suggests that mixture toxicity would not result in significant cumulative effects.

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Appendix: Risk Estimation for Accidental Occupational Dermal Exposure

Parameters	Units	Values		Sources
Dose = PDR/BW	mg/kg-d	0.000585	0.00117	USEPA 2007
		0.000250714	0.000501429	
		0.00019102	0.000382041	
BW=body weight	kg	70	70	USEPA 2011
PDR = UE * AR * A	mg/day			
PDR =Daily potential dose rates	mg/lb a.i	0.04095	0.0819	
		0.01755	0.0351	
		0.013371429	0.026742857	
UE = unit exposure (mg/lb ai)	mg/lb a.i	1.3	1.3	USEPA 2013d
AR = maximum application rate (lb ai/acre or lb ai/gal)	lb ai/acre	0.0045	0.009	Label
A = maximum area treated (acre/d or gal/d)	acres/days	7	7	
		3	3	
		2.285714286	2.285714286	
Hours of application per day	hrs/day	7	7	
		6	6	
		8	8	
Acres treated per hour	acres/hrs	1	1	Estimated based on label
		0.5	0.5	
		0.285714286	0.285714286	
Oral RfD (occupational)	mg/kg/day	0.27	0.27	
Hazard Quotient		0.002	0.004	
		0.0009	0.002	
		0.0007	0.001	