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Draft Human Health and Ecological Risk Assessment for Malathion in Exotic Fruit Fly Applications

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EXECUTIVE SUMMARY

The United States Department of Agriculture (USDA), Animal and Plant Health Inspection Service (APHIS), Plant Protection and Quarantine (PPQ) is proposing to use malathion in its cooperative exotic fruit fly eradication program. Malathion is a non-systemic, wide spectrum, organophosphate insecticide contained in a bait spray that is applied using ground or aerial equipment.

USDA-APHIS evaluated the potential human health and ecological risks from the proposed use of malathion and determined that the risk to human health and the environment is minimal. USDA-APHIS finds minimal risk to human health and the environment based on the low probability of exposure to people and the environment by adherence to label requirements and the proposed use pattern. USDA-APHIS does not expect adverse health risks to workers based on the low potential for exposure to malathion during applications according to label directions and use of personal protective equipment. The worse-case scenario involves accidental exposure to malathion during application (mixing and loading) by workers. The quantitative evaluation for the accidental exposure did not find a risk level of concern. USDA-APHIS does not expect adverse health risks to the public because program malathion treatments are restricted to commercial plantings, there is a notification process that occurs in advance of the treatment and the program implements the label required restricted entry and post-harvest intervals.

Malathion may pose a risk to some aquatic invertebrates and vertebrates; however, the use of a large droplet size, low use rates, and other label precautions will reduce risk. Risks to terrestrial non-target vertebrates and invertebrates will be greatest within the treatment block, but the off-site risk is considered low based on conservative risk estimates. Risk to sensitive non-target vertebrates and invertebrates within the spray block will be reduced by the use of a large droplet size and a fruit fly attractant that allows for low use rates that are more attractive to the target pest.

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, invertebrates, and wildlife as a result of exposure to malathion under the proposed aerial or ground applications of malathion bait spray to eradicate various species of exotic fruit flies (e.g., Mediterranean fruit fly, Mexican fruit fly, Oriental fruit fly, etc.) when they enter the United States.

The methods used to assess potential human health effects follow standard regulatory guidance and methodologies (NRC, 1983; USEPA, 2016a), 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), an effects analysis (the dose-response assessment), and an exposure assessment (identifying potentially exposed populations and determining potential exposure pathways for these populations). The fourth section (risk characterization), integrates the information from the exposure assessment and effects analysis to characterize the risk of malathion 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 these pest species 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 exotic fruit fly species establish in these areas (USDA APHIS, 2013).

Malathion is a broad-spectrum organophosphate insecticide widely used to control insects such as aphids, leafhoppers, and Japanese beetles in agriculture for various food and feed crops with the predominant use on cotton (USEPA, 2009, 2016b). Other significant agricultural uses include alfalfa hay, other hay, cherries, strawberries, lettuce, citrus fruit, blueberries, wheat, and walnuts. Residential uses of malathion include outdoor applications to vegetable gardens, perimeter house treatments, home orchards, and ornamentals. Municipal vector control programs use malathion for public health adult mosquito control. USDA-APHIS uses malathion in the Fruit Fly Eradication Program, as well as the Boll Weevil Eradication Program and the Grasshopper and Mormon Cricket Suppression Program.

Malathion affects the nervous system through acetylcholinesterase (AChE) inhibition. Malathion is converted to its oxon metabolite, malaoxon, which is a more potent AChE inhibitor than malathion (approximately 22 times as toxic as malathion in mammals) (USEPA, 2016b). USDA-APHIS uses a mixture of malathion and a protein hydrolysate bait to control fruit flies for its fruit fly eradication program.

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

2.1 Chemical Description and Product Use

Malathion (CAS No. 121-75-5, $C_{10}H_{19}O_6PS_2$) is the common name for O,O-dimethyl thiophosphate of diethyl mercaptosuccinate. The chemical structure is illustrated in figure 2-1. The chemical structure for malaoxon (CAS No. 1634-78-2, $C_{10}H_{19}O_7PS$) is illustrated in figure 2-2.

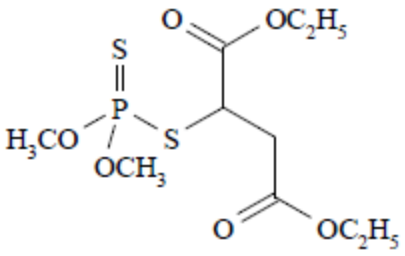

Figure 2-1 The chemical structure of malathion

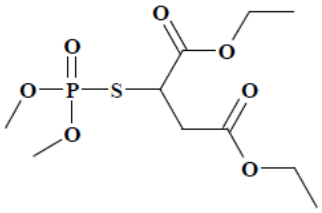

Figure 2-2 The chemical structure of malaoxon

USEPA first registered malathion as an insecticide in 1956. The program proposed formulation (Malathion 8 Aquamul) (EPA Reg. No. 34704-474) contains 81.8% malathion as the active ingredient (a.i.) and 18.2% other ingredients (8 pounds malathion per gallon) (Loveland Products, Inc., 2015). The proposed use of a malathion bait spray consists of 2.8 fluid ounces of the formulation (0.18 pounds of a.i.) mixed with 9.6 fluid ounces of protein hydrolysate bait per acre. Malathion bait spray is applied by ground or air broadcast treatments. The program conducts applications in accordance with the Section 3 label for Malathion 8 Aquamul and Section 24(c) registrations used to control fruit flies in California (SLN No. CA830012) and Florida (SLN No. FL150006).

2.2 Physical and Chemical Properties

Malathion is a colorless to amber liquid with a mercaptan odor. It has a molecular weight of 330.4 g/mol and a boiling point of 156–157 ºC. Its vapor pressure is 4.0 x 10^{-5} mm Hg at 30 ºC. The Henry's law constant of malathion is 1.2 x 10^{-7} atm-m^3/mol at 25 ºC. Malathion is soluble in water with a water solubility of 145 mg/L at 25 ºC and is readily soluble in most alcohols and esters, but is only slightly soluble in aliphatic hydrocarbons. Its log octanol-water partition coefficient ranges between 2.29 and 3.30, and the organic carbon normalized partition coefficient (Koc) ranges between 151 (sandy loam) and 308 (sand) (USEPA, 2009, 2016b).

Malaoxon is the primary metabolite and an environmental breakdown product of malathion. Malaoxon has a molecular weight of 314.29 g/mol and a boiling point of 114 ºC. Its vapor pressures range from 2.45 x 10^{-6} to 3.2 x 10^{-4} torr (10–50 ºC) and water solubility is 0.5–1.0 g/100 mL (22 ºC) (USEPA, 2016b). Malaoxon has a Koc of 46 L/kg (USEPA, 2009).

2.3 Environmental Fate

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

Malathion from ground or aerial applications can be transported into the atmosphere through drift and volatilization as well as by fog and wind. Malathion has limited photolysis potential in the environment because the absorbed electro-magnetic spectrum of malathion is not within the range of natural sunlight. Malathion is not persistent in soil. Aerobic metabolism appears to be the primary route of degradation in surface soils. The aerobic half-lives of malathion in soil range from several hours to approximately 11 days. Malathion is less persistent in the presence of microbial activity, moisture, and high pH. Malathion does not adsorb strongly to soils and is soluble in water. As a result, malathion can be highly mobile and migrate to surface water via runoff and groundwater via leaching. However, the short persistence of malathion in soil reduces the likelihood of groundwater leaching (USEPA, 2009, 2016b).

Malathion's degradation in water is pH dependent. It is non-persistent under alkaline conditions with hydrolysis as the main degradation route. Malathion is hydrolytically stable under acidic aqueous conditions (a half-life of 107 days at pH 5) and becomes unstable under alkaline conditions and hydrolyzes rapidly (half-lives of 6.21 days and 12 hours in the pH of 7 and 9 solutions, respectively) (USEPA, 2009).

Malathion can break down to degradation products such as malaoxon, malathion alpha and beta monoacid, diethyl fumarate, diethyl thiomalate, and O,O-dimethylphosphorodithioic acid through hydrolysis (Newhart, 2006). Among these degradates, only malaoxon is sufficiently toxic in the environment (USEPA, 2016b). Malathion in soil generally degrades rapidly to compounds of lower toxicity. However, some studies indicate that malathion degrades to malaoxon under dry and microbially inactive environmental conditions such as on dry soil (USEPA, 2009). The half-life values for malaoxon in soil range from 3–7 days (US FS, 2008; Bradman et al., 1994). USEPA reports an aerobic soil half-life of 21 days for malaoxon that was used to model environmental concentrations in water (USEPA, 2016b).

Malathion in plants metabolizes through oxidation to form malaoxon and de-esterification to form mono- and dicarboxylic acids and succinate derivatives (USEPA, 2016b). Malathion on plant surfaces has a half-life ranging from <0.3 to 8.7 days (Newhart, 2006).

Fish malathion bioconcentration factor (BCF) values are low: 4.2 to 18, 37 to 204, and 23 to 135 in edible, viscera, and whole fish, respectively (USEPA, 2009). Malathion is not expected to bioconcentrate or biomagnify because it is quickly eliminated from fish when moved to clean water (Tsuda et al., 1989; Deka and Mahanta, 2016).

2.4 Hazard Identification

Malathion is a hazard to human health primarily due to its direct effects on the nervous system. Clinical signs of neurotoxicity include tremors, salivation, urogenital staining, and decreased motor activity (USEPA, 2016b). Exposure to high levels of malathion may cause difficulty breathing, chest tightness, vomiting, cramps, diarrhea, watery eyes, blurred vision, salivation, sweating, headaches, dizziness, loss of consciousness, and death (ATSDR, 2003).

2.4.1 Toxicological Effects

Similar to other organophosphate pesticides, malathion inhibits the enzyme AChE in the central and/or peripheral nervous system (USEPA, 2016b). Malathion is metabolized to malaoxon, which is the active AChE inhibiting metabolite. AChE inhibition is through phosphorylation of the serine residue at the active site of the enzyme, and leads to accumulation of acetylcholine and ultimately neurotoxicity. The available studies indicate red blood cell AChE inhibition is more sensitive to malathion exposures than brain AChE inhibition after oral and dermal exposure. After inhalation exposure, the observed toxicity effects include histopathologic lesions of the nasal cavity and larynx.

2.4.2 Absorption, Distribution, and Excretion

Malathion will generally absorb and distribute rapidly with extensive metabolism and no accumulation in tissues (USEPA, 2016b). Carboxylesterase detoxifies malathion and malaoxon to polar and water-soluble compounds for excretion. A rat metabolism study showed 80 to 90% of malathion excretion in the urine in the first 24 hours of exposure. Mammals are less sensitive to the effects of malathion than insects due to greater carboxylesterase activity resulting in less accumulation of malaoxon.

2.4.3 Human Incidents

This section is a summary of reviews by the USEPA/OPP Health Effect Division (HED) on acute pesticide poisoning surveillance data for malathion, chronic disease epidemiology, and registrant submitted evaluations of certain environmental and occupational epidemiology data (2016b).

The HED's review of acute pesticide surveillance data indicates that acute exposure to malathion causes organophosphate acute toxicity including neurological, gastrointestinal and respiratory effects. These acute adverse health effects are generally mild to moderate and are reversible with primary medical intervention. However, medical case reports indicate that exposure to malathion at sufficiently high doses from accidental or intentional misuse can cause severe acute cholinergic crisis, intermediate syndrome, organophosphate induced delayed neuropathy, and a Parkinson's-like syndrome.

The HED's review on the epidemiology database indicates there is no evidence of an association with specific malathion use in the majority of the studies with health effects. Studies of the potential carcinogenic effects from malathion exposure in the human population did not show compelling evidence that malathion plays a role in the development of cancers, such as total prostate cancer, Hodgkin lymphoma, and soft tissue sarcoma. The HED reviews (USEPA, 2014a, 2016c) suggest a need for additional studies on several malathion-chronic disease associations. For example, there is a need for replication in a study population external to the Agricultural Health Study (AHS, https://aghealth.nih.gov/) for the suggestive association of malathion exposure with an aggressive form of prostate cancer. There is also a need for prospective studies of the association between chronic pesticide exposure and lymphohematopoietic cancer (such as leukemia and multiple myeloma).

Studies regarding the potential role of malathion exposure and adverse respiratory health effects in the AHS database indicate some evidence of a statistical association among malathion use and wheezing, asthma, and chronic bronchitis. Studies of in-utero malathion exposure (maternal urinary concentration of malondialdehyde) and birth outcomes (e.g., birth weight and length), adverse neurodevelopmental effects, and birth defects listed in the AHS database did not show evidence of a positive statistical association between malathion exposure and adverse birth outcomes or developmental effects. The HED's review noted there is only one study of this particular association, although a prospective cohort study (Mt. Sinai birth cohort study) reported a significant association with malathion exposure and the number of abnormal reflexes in the exposed neonate.

There is no statistical evidence supporting an association between malathion exposure with myocardial infarction; hyper- and hypo-thyroid disease; retinal degeneration; Parkinson's disease; neurological functioning in adults; and male reproductive effect (semen parameters). Insulin resistance and diabetes, in contrast, may have a significant association with malathion, although the HED's review suggests a need for additional research.

2.4.4 Acute Toxicity

Malathion has low acute dermal toxicity (Toxicity Category III) and very low acute oral and inhalation toxicities (Toxicity Category IV). The acute oral median lethal dose (LD_{50}) in rats is 5,400 milligrams/kilogram (mg/kg) (males) and 5,700 mg/kg (females) (Toxicity Category IV). The acute dermal LD_{50} in rats exceeds 2,000 mg/kg for both males and females (Toxicity Category III). The acute inhalation median lethal concentration (LC_{50}) in rats exceeds 5.2 mg/liter (L) for both males and females (Toxicity Category IV). Malathion causes slight eye conjunctival irritation in rabbits that clears in seven days (Toxicity Category III), and slight dermal irritation in rabbits (Toxicity Category IV). It is not a dermal sensitizer in guinea pigs (USEPA, 2009).

2.4.5 Subchronic and Chronic Toxicity

A 21-day dermal toxicity study in rabbits (94%, a.i.) reported a benchmark dose ($BMDL_{20}$[1]) of 135/143 mg/kg/d (male/female (M/F)). Another 21-day dermal toxicity study in rabbits (96%, a.i.) reported a) a $BMDL_{10}$[2] of 80 mg/kg/d (females) and BMD_{10} of 124 mg/kg/d with no model fit for male data at BMD_{10} level, and b) a $BMDL_{20}$ of 92.2/119.6 mg/kg/day (M/F) and a BMD_{20} of 123.9/145.2 mg/kg/day (M/F). The $BMDL_{10}$ is the lower confidence bound on the BMD_{10}. The $BMDL_{20}$ is the lower confidence bound on BMD_{20}. Dermal irritation was observed at all doses (USEPA, 2016b).

A 90-day inhalation study in the rat (96.4%, a.i.) reported a lowest observable adverse effect level (LOAEL) of 0.1 mg/L based on histopathological lesions of the nasal cavity and larynx in males and females. A red blood cell AChE inhibition effect, $BMDL_{10}$ is 0.082/0.049 mg/L (M/F), and BMD_{10} is 0.167/.0126 mg/L (M/F) (USEPA, 2016b).

A chronic toxicity study in dogs (95%, a.i.) reported a systemic no observed adverse effect level (NOAEL) of >250 mg/kg/day (highest dose tested). The AChE inhibition NOAEL was not established; however, the plasma and red blood cell AChE inhibition LOAEL was <62.5 mg/kg/day.

2.4.6 Nervous System Effects

Neurotoxicity (AChE) inhibition in red blood cells is the most sensitive endpoint of malathion exposure in all species without a difference in sex, and is the critical endpoint in oral and dermal exposures. Malathion also causes AChE inhibition in inhalation exposure. USEPA's point of departure for inhalation is based on histopathological lesions of the nasal cavity and larynx effects because of a lower observed dose than the one causing AChE inhibition (USEPA, 2016b).

Studies of acute delayed neurotoxicity or structural neuropathy caused by malathion exposure have been negative (USEPA, 2016b). Acute and subchronic neurotoxicity studies using the rat resulted in no observed adverse effect level (NOAEL) values of 1,000 mg/kg and 4 mg/kg/day, respectively. The acute and subchronic lowest observed effect levels (LOAEL) were 2,000 mg/kg based on decreased motor activity, clinical signs and plasma and red blood cell AChEI while the subchronic LOAEL was 352/395 mg/kg/day (M/F) based on inhibition of plasma and brain AChE activity. Results from a developmental neurotoxicity study revealed a maternal NOAEL of 50 mg/kg/day and a LOAEL of 150 mg/kg/day based on an increased incidence of post-dosing salivation, and an offspring NOAEL of 50 mg/kg/day and a LOAEL of 150 mg/kg/day based on clinical signs (such as whole body tremors, hypoactivity, prostrate posture, and partially closed eyelids), and brain morphometrics.

[1] $BMDL_{20}$ is defined as the lower 95% confidence interval for the estimated mean dose at which 20% red blood cell AChE inhibition is observed.
[2] $BMDL_{10}$ is defined as the lower 95% confidence interval for the estimated mean dose at which 10% red blood cell AChE inhibition is observed.

2.4.7 Reproductive or Developmental Effects

A two-generation reproduction study in rats using 94% malathion a.i. reported a parental NOAEL of 394/451 mg/kg/day (M/F), and a LOAEL of 612/703 mg/kg/day (M/F) based on decreased F_0 generation body weights during gestation and lactation (females) and decreased F_1 pre-mating body weights (M/F). The offspring NOAEL was 131/153 mg/kg/day (M/F). The offspring LOAEL was 394/451 mg/kg/day (M/F) based on decreased pup body weights during the late lactation period in F_1 and F_2 pups.

The developmental toxicity study in rats (94% a.i., administered doses of 0, 200, 400, 800 mg/kg/day) reported a maternal NOAEL of 400 mg/kg/day and a maternal LOAEL of 800 mg/kg/day based on reduced mean body weight gains and reduced mean food consumption. The developmental NOAEL was 800 mg/kg/day, and the developmental LOAEL was >800 mg/kg/day with no adverse developmental effects observed at the highest dose tested (USEPA, 2016b).

The developmental toxicity study in rabbits (92.4% a.i., administered doses of 0, 25, 50, 100 mg/kg/day) reported a maternal NOAEL of 25 mg/kg/day, and a maternal LOAEL of 50 mg/kg/day, based on reduced mean body weight gains during days 6–18 of gestation. The developmental NOAEL was 25 mg/kg/day and the developmental LOAEL was 50 mg/kg/day based on an increased mean number of resorption sites/dose (USEPA, 2016b).

The developmental toxicity studies in rat and rabbit did not indicate evidence of quantitative and/or qualitative adverse developmental effects at >800 mg/kg/day (the highest dose tested), or developmental effects that can be attributed to fetal or maternal toxicity. The reproduction study in rats observed quantitative susceptibility of decreased pup body weights during the lactation period in the F_{1a} and F_{2b} pups without maternal toxicity. The developmental neurotoxicity study observed qualitative susceptibility with clinical signs (such as whole body tremors, hypoactivity, prostrate posture, partially closed eyelids) and brain morphometrics (such as increased thickness of the corpus callosum) in offspring animals with limited maternal effects (such as post dosing salivation) (USEPA, 2016b).

2.4.8 Carcinogenicity and Mutagenicity

The International Agency for Research on Cancer concluded malathion is probably carcinogenic to humans (Group 2A) based on sufficient evidence in experimental animals, but limited evidence for cancer in humans with positive associations observed for non-Hodgkin lymphoma and cancer of the prostate (IARC, 2016). Other strong supportive evidence includes: 1) malathion-based pesticides are genotoxic based on studies in humans, in experimental animals, and in human and animal cells in vitro; 2) malathion modulates receptor-mediated effects and pathways relevant to tumor findings in the hormone-responsive tissues, the thyroid, and mammary gland; 3) alteration of cell proliferation in response to malathion in these tissues; and 4) malathion induces oxidative stress and inflammation based on the most extensive database

from in-vivo studies in experimental animals. Oxidative stress was also demonstrated in human cells in vitro and in a study of humans acutely poisoned with malathion-based pesticides.

USEPA classifies malathion as having "suggestive evidence of carcinogenicity but not sufficient to assess human carcinogenic potential" (USEPA, 2016b). Mutagenicity studies (such as bacterial and mouse gene mutation, mammalian bone marrow chromosome aberration, and unscheduled DNA synthesis in rat) are not supportive of mutagenic concern in carcinogenicity.

2.4.9 Endocrine System Effects

Malathion was one of 52 chemicals to undergo Tier 1 screening for endocrine disruptor potential under the USEPA Endocrine Disruptor Screening Program (EDSP) (USEPA, 2015). Based on the Tier 1 assay data, and other scientifically relevant information, including general toxicity data and open literature studies of sufficient quality, USEPA (the EDSP Tier 1 Assay Weight of Evidence Review Committee of the USEPA/OPP and the Office of Science Coordination and Policy) performed a weight–of-evidence assessment of the potential interaction of malathion with the estrogen, androgen, or thyroid hormone signaling pathways. The weight-of-evidence analysis concluded there was no convincing evidence for the potential interaction of malathion with estrogen, androgen, or thyroid pathways. As a result, mammalian and wildlife EDSP Tier 2 testing was not recommended (USEPA, 2015).

2.4.10 Immune System Effects

Some studies indicate that malathion may affect the immune system (ATSDR, 2003, US FS, 2008). A recent USEPA guideline immunotoxicity study in mice reported a NOAEL of 1,215.8 mg/kg/day (7,000 parts per million (ppm), highest dose tested) for immunotoxicity without the establishment of a LOAEL. The study also reported a systemic toxicity NOAEL of 17.6 mg/kg/day (100 ppm) and a LOAEL of 126.8 mg/kg/day (700 ppm) based on statistically significant reductions in red blood cell cholinesterase activity (USEPA, 2016b).

2.4.11 Toxicity of Other Ingredients

The Loveland Products safety data sheet (2016) lists 18.2% other ingredients in the malathion formulation used by the program. Specific compounds are not listed for these ingredients and are considered confidential business information. Available acute toxicity data using the formulated material suggests comparable toxicity to the active ingredient. The Malathion 8 Aquamul formulation has low acute oral, dermal, and inhalation toxicities (Toxicity Category III or IV). The safety data sheet (Loveland Products, Inc., 2016) reported an acute oral LD_{50} of >550 mg/kg (III), an acute dermal LD_{50} of >2,000 mg/kg (III), and an acute inhalation LC_{50} of >5.1 mg/l in a 4-hour exposure (IV) to rats. The Malathion 8 Aquamul formulation is a mild skin irritant and causes moderate eye irritation in rabbits, and is a skin sensitizer in guinea pigs.

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.

For an acute dietary exposure of all populations, the USEPA/OPP selected a point of departure (POD) of 10 mg/kg/day, and an acute population adjusted dose (aPAD) of 0.01 mg/kg (acute reference dose (aRfD) = 0.1 mg/kg) for exposure scenarios with infants, children, youth, and women of childbearing age. An uncertainty factor (UF) of 1000X (10X for interspecies extrapolation, 10X for intraspecies variation and 10X for the Food Quality Protection Act (FQPA) safety factor (SF) due to uncertainty in the human dose-response relationship for neurodevelopmental effects) was applied to the POD. The aPAD for the population subgroup of adults 50-99 years old is 0.1 mg/kg/day (aRfD= 0.1 mg/kg) because of a FQPA SF of 1 (USEPA, 2016b).

To account for the increased toxicity from exposure to malaoxon, USEPA applied a toxicity adjustment factor of 22, because malaoxon is 22X more toxic than malathion.

Malathion is classified as “suggestive evidence of carcinogenicity, but not sufficient to assess human carcinogenic potential”. USEPA assumes that “quantification of risk using a non-linear approach (i.e., the chronic reference dose) will adequately protect for chronic toxicity including carcinogenicity” (USEPA, 2016b).

USEPA sets tolerance levels (the amount of pesticide residue allowed to remain in or on each treated food commodity) using dietary risk assessments (USEPA, 2016d). The USEPA established a tolerance of 1 ppm for residues of malathion (including its metabolites and degradates) in or on all raw agricultural commodities from uses for pest (mosquito and fly) control areas (USEPA, 2016b).

3.2 Ecological Dose-Response Assessment

3.2.1 Wild Mammal, Avian and Reptile Toxicity

The acute oral median lethal doses for birds range from 150 mg/kg for chickens to 1,485 mg/kg for mallard ducks (Hudson et al., 1984). The 5-day dietary median lethal concentrations ranged from 2,639 ppm for the ringed neck pheasant to greater than 5,000 ppm for the mallard (table 3-1).

Table 3-1. Acute oral and dietary toxicity of malathion to birds.

Test Species	Endpoint	Toxicity Value	Reference
Red-winged blackbird, *Agelaius phoeniceus*	LD_{50}	400 mg/kg	Schafer et al., 1983
Sharp-tailed grouse, *Tympanuchus phasianellus*	LD_{50}	220 mg/kg	USEPA, 2006a
Ring-necked pheasant, *Phasianus colchicus*	LD_{50}	167 mg/kg	USEPA, 2006a
Horned lark, *Eremophila alpestris*	LD_{50}	403 mg/kg	USEPA, 2006a
Mallard duck, *Anas platyrynchos*	LD_{50}	1,485 mg/kg	Hudson et al., 1984
Ring-necked pheasant (male), *Phasianus colchicus*	LC_{50}	2,639 ppm	USEPA, 2006a
Northern bobwhite quail, *Colinus virginianus*	LC_{50}	3,497 ppm	USEPA, 2006a
Japanese quail, *Coturnix japonica*	LC_{50}	2,962 ppm	USEPA, 2006a
Mallard duck, *Anas platyrynchos*	LC_{50}	>5,000 ppm	USEPA, 2006a

Several reproductive and developmental studies have been conducted with birds. The lowest median lethal dose to chicken embryos (eggs) was 3.99 mg per egg for 4-day embryos (Greenberg and LaHam, 1969). The median lethal concentration for field applications of malathion to mallard duck eggs was found to be 4.7 lbs a.i./acre (Hoffman and Eastin, 1981).

No effect on reproductive capacity of chickens was found at dietary concentrations as high as 500 ppm in feed (Lillie, 1973). Based on the results from chronic reproduction studies using the bobwhite quail and mallard duck, the NOEC values were 110 and 1,200 ppm, respectively. The most sensitive endpoint in the quail study was regressed ovaries and reduced egg hatch at the next highest test concentration (350 ppm). The effect endpoint in the mallard study was growth and egg viability at the 2,400 ppm level (LOEC).

Sub-chronic and chronic studies have also been conducted on surrogate avian species assessing AChE inhibition. Significant inhibition of AChE (40–60%) can lead to several sublethal effects such as lack of coordination and behavioral effects. Meydani and Post (1979) dosed Japanese quail daily for 21 days at 20, 40, and 75 mg/kg/day and then measured brain AChE and flying activity at day 0, 10, 20, and 30 after the last day of dosing. At 20 mg/kg/day, there was an approximate 26% reduction in brain AChE activity. The authors did not conduct a statistical analysis so it is unknown whether this value was statistically significant. Dieter (1975) dosed European starlings, *Sturnus vulgaris*, daily in feed for 12 weeks and found a statistically significant effect on cholinesterase activity at 35 ppm but not at 160 ppm.

Day et al. (1995) examined the potential immunotoxic effects of malathion on 8-week old ring-necked pheasants, *Phasianus colchicus*, by dosing birds once at a concentration of 92 and 230 mg/kg. Decreases in thymic and splenic weights were observed at the highest test concentration.

Laboratory toxicity testing using reptiles is less extensive than data available for other non-target vertebrates. Holem et al. (2006) noted 20% mortality in the western fence lizard (*Sceloporus occidentalis*) after oral dosing of 200 mg/kg of Fyfanon® ULV. Approximately 70% of the dosed lizards demonstrated clinical signs of organophosphate toxicity. In addition to measuring

mortality, sprint performance was assessed to determine potential locomotor effects to reptiles after malathion exposure. No effects on sprint performance were noted at the 0.2 and 2.0 mg/kg dose rate; however, there was a 23% increase in sprint velocity at 20 mg/kg. In another study using the same species repeated malathion exposures resulted in 8% and 23% mortality at 20 and 100 mg/kg, respectively. In the 100 mg/kg group, 85% of lizards showed clinical symptoms of poisoning as well as significantly reduced arboreal sprint velocity or refused to sprint in the arboreal setting (Holem et al., 2008). Hall and Clark (1982) found significant effects on cholinesterase activity in green anoles (*Anolis carolinensis*) at 648 mg/kg with significant effects on mortality at 3,000 mg/kg.

3.2.2 Terrestrial Invertebrate Toxicity

A large amount of data exists regarding the toxicity of malathion to terrestrial invertebrates. However, comparing toxicity values between the different studies is problematic because dosing is not standardized relative to other non-target testing, and the doses can be presented in numerous units. Based on the various toxicity studies that are available, malathion is moderately to severely toxic to terrestrial invertebrates. The median lethal concentration of malathion to earthworms ranges from 0.27 to 13.5 microgram (µg)/cm^2 (Roberts and Dorough, 1985). The reported LD_{50} for earthworms based on malathion dosing in soil was found to be 600 mg a.i./kg soil with a reported NOEC of 80 mg/kg (Espinoza-Navarro and Bustos-Obregon, 2004).

The range of contact LD_{50} values in honeybees ranges from 0.20 to 0.70 µg/bee (US FS, 2008). The alkali and alfalfa leafcutter bee appear to be similar in sensitivity with contact LD_{50} values of 0.31 and 0.47 µg/bee, respectively (USEPA, 2012). Plant residue toxicity studies using the honeybee revealed a NOEC value of 1.6 lb a.i./ac, suggesting malathion is more toxic from direct contact compared to exposure from malathion residues on plants.

Median lethal concentrations of malathion to insects range from 2.39 mg/kg for some lepidopteran species to 23 mg/kg for carpenter ants (Gibson and Scott, 1989; Pree et al., 1989) and up to 124.1 mg/kg for lacewings. Aikins and Wright (1985) reported a range of LC_{50} values of 3.3 to 102 µg/g organism based on 24-hour exposures using the cabbage moth, *Mamestra brassicae*. Leonova and Slynko (2004) reported differential toxicity in 5th instar larvae and adults of the beet webworm, *Loxostege sticticalis*, with 24-hour reported LD_{50} values of 2,320 and 2.39 µg/g, respectively.

Mansee and Montasser (2003) reported the 120-hour LC_{50} value to be 4.42 and 1.89 µg/cm^2 for the red flour beetle, *Tribolium castaneum*, based on exposures in light and dark environments. Khalequzzaman and Nahar (2001) reported a 24-hour LC_{50} value of 8.06 µg/cm^2 for *T. castaneum*. In another study using *T. castaneum*, the reported LC_{50} value for malaoxon was approximately 14 times more toxic to beetles than the parent (Haubruge et al., 2002).

USEPA (2007) reported 7-day NOEC values for Coleoptera and Hymenoptera of 1,300 g a.i./ha or 1.16 lb a.i./ac.

3.2.3 Terrestrial Plant Toxicity

Malathion has low phytotoxicity to most plants. Concentrations above program application rates are required for adverse effects to conifers, clover, and pea plants (Archer, 1971; Chakraborti et al., 1983; Ilnytzky and Marshall, 1974). A variety of agronomically important crops have been tested at rates higher than those used in the program with no known phytotoxic effects.

3.2.4 Aquatic Vertebrate Toxicity

The acute toxicity of malathion varies from moderately toxic to some species of fish to very highly toxic to other species, with an LC_{50} of 4 µg/L in rainbow trout to 15,300 µg/L for the federally listed bonytail chub, *Gila elegans* (Beyers et al., 1994; Mayer and Ellersieck, 1986; US FS, 2008) (figure 3–1; appendix B-1).

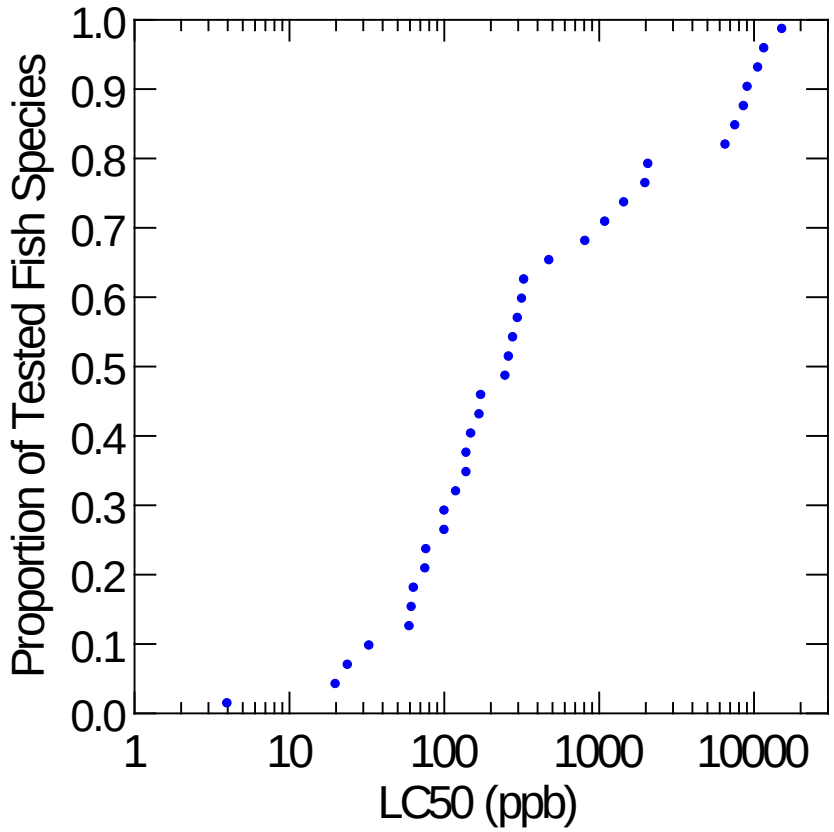

Figure 3-1. Acute toxicity of malathion to freshwater and saltwater fish species

An analysis of the relative toxicity of malathion to taxonomic families of fish (Macek and McAllister, 1970) determined that the least susceptible families include catfish and minnows, and the more susceptible families include trout, salmon, perch, and sunfish.

Several acute sublethal and chronic laboratory toxicity studies are available for malathion using freshwater and saltwater fish species.

Beyers and Sikoski (1994) determined a cholinesterase inhibition based NOEC of 371 µg/L during a 24-hour exposure to the federally listed Colorado squawfish (*Ptychocheilus lucius*). In another study, Beyers et al. (1994) determined the acute 96-hour NOEC for *P. lucius* and *G. elegans* for growth to be 1,680 µg/L and 990 µg/L, respectively, for each species. Beauvais et al. (2001) noted changes in four measured swimming responses of rainbow trout after exposure to 20 and 40 µg/L malathion during 24- and 96-hour exposures. Lower concentrations were not tested; therefore, no NOEC could be determined. These effects were correlated with cholinesterase inhibition that was detected during the study. Richmonds and Dutta (1992) measured cholinesterase activity in bluegill during a 24-hour exposure and determined the NOEC and LOEC to be 8.0 and 16 µg/L, respectively, based on a statistically significant inhibition of brain cholinesterase activity. In another acute sublethal exposure study, Cook et al. (2005) exposed zebrafish embryos for 120 hours to a range of malathion concentrations (0.5–3.0 mg/L) and measured survival, hatching, body length, and eye diameter. Concentrations where each response was not statistically significant were 2.0, 2.0, 1.5, and 0.5 mg/L for survival, hatching, body length, and eye diameter, respectively. Eye diameter effects were also noted in the solvent control.

In a 97-day continuous exposure study using the rainbow trout, the NOEC was determined to be 21 µg/L, while the LOEC was 44 µg/L (USEPA, 2006a). In another chronic study, the flagfish (*Jordanella floridae*) was exposed during a 110-day period with a resulting NOEC value of 8.6 µg/L (USEPA, 2006a). In a review of reproductive and behavioral studies conducted with malathion, USEPA reported a reproductive NOEC of 20 µg/L for the bluegill after an 8-week exposure, based on effects to adult survival and egg production. Spinal deformations were also observed at several concentrations with a reported maximum acceptable toxicant concentration of 3.6 to 7.4 µg/L. In another study review by USEPA, sheepshead minnow (*Cyprinodon variegatus variegatus*) embryos were exposed to a range of malathion concentrations to determine the potential for abnormal swimming behavior associated with skeletal malformations. Effects were seen at 3 mg/L and 10 mg/L, with a resulting NOEC of 1.0 ppm (USEPA, 2006a).

Acute toxicity to amphibians is variable based on the sensitivity of different species and time of exposure. Relyea (2004) tested the survival rates of six species of tadpoles over a 16-day exposure period to a malathion formulation. Testing wood frogs, *Rana sylvetica*; leopard frogs, *R. pipens*; green frogs, *R. clamitans*; bullfrogs, *R. catesbiana*; American toads, *Bufo americanus*; and gray tree frogs, *Hyla versicolor*, the reported 16-day LC_{50} values were 5.9, 3.7, 2.4, 2.0, 1.5, and 1.3 mg/L, respectively, for each species. Survival was also measured in the presence of a predator, and there was no interaction between predation and chemical exposure for any of the test species with the exception of *H. versicolor* where lethality was greater in the presence of predator stress. Reported 24- and 96-hour LC_{50} values for Woodhouse's toad, *Bufo woodhousei*, are 1.9 and 0.42 mg/L, respectively while values reported for the western chorus frog, *Pseudacris triseriata*, are reported as 0.56 and 0.20 mg/L (Mayer and Ellersieck, 1986).

Gurushankara et al. (2003) reported 24-, 48-, 72-, and 96-hour LC_{50} of 13.27, 8.73, 6.3, and 5.37 ppm for the Indian cricket frog, *Limnonectus limnocharis*.

Several studies have been conducted to assess the sublethal acute and chronic effects of malathion exposure to amphibians. Fordham et al. (2001) exposed bullfrog (*R. catesbiana*) tadpoles for 28 days with technical grade malathion at concentrations ranging from 0.5 to 3.0 mg/L. Survival was significantly lower at concentrations of 2.5 mg/L and higher, while developmental delays at the 1.0 mg/L concentrations and higher were noted. Loss of equilibrium posture, which could affect predation and feeding, were noted at all concentrations. In another 28-day exposure, Gurushankara et al. (2007) reported significant effects on *L. limnocharis* body weight, length, and food consumption after exposure to a formulation of malathion. Based on a graphical interpretation of the data, it appears that statistically significant effects were noted at 1.0 mg/L and higher for all endpoints with the exception of food consumption, which was shown in the study to be statistically reduced at concentrations of 1.5 mg/L and above. The estimated NOEC for all endpoints was 0.5 mg/L with the exception of food consumption which was 1.0 mg/L. Taylor et al. (1999) applied formulated malathion topically to adult male Woodhouse's toads (*B. woodhousi*) at rates of 0.011 and 0.0011 mg malathion/g toad and found a higher mortality rate when the toads were challenged with sublethal intraperitoneal doses of the bacterium, *Aeromonas hydrophila*. The lethal dose in the study was calculated as 0.11 mg malathion/g toad and based on the maximum use rate listed in the study the toads would have to be exposed to the amount of malathion applied over a 2-meter area. Mohanty-Hejmadi and Dutta (1981) reported limb bud-stage and metamorphosis related effects to the Indian bullfrog, *Hoplobatrachus tigerinus,* at nominal concentrations ranging from 1.5 to 3.5 mg/L in a static renewal study where solutions were changed twice a week for an unstated time period.

There is data to suggest that malathion may have teratogenic effects to developing frog embryos of *Microhyla ornata*, when concentrations exceed 1 mg/L of a 50% emulsifuable concentrate formulation of malathion (Pawar, 1983). Effects included spinal curvature and abnormal swimming behavior at concentrations ranging from 5 to 10 mg/L. At concentrations greater than 10 mg/L, malathion was highly embryo-toxic. Rosenbaum et al. (1988) studied the effects of malathion exposure to embryos of the South American toad, *Bufo arenarum*. At exposure levels ranging up to 30 mg/L, embryonic development appeared normal. At the 44 mg/L exposure level, 67% mortality was observed after 5 days exposure compared to 8% mortality in control embryos. De Llamas et al. (1985) did not note developmental related effects to *B. arenarum* embryos after exposure to 0.47 mg/L malathion; however, embryogenesis was interrupted at 47.3 mg/L.

Studies of adult salamanders and lizards exposed to field applications (up to 6 oz a.i./acre) of malathion found no observable adverse effects and no AChE inhibition (Baker, 1985; McLean et al., 1975). In a behavior experiment, no effects on feeding, endurance, and coordination were noted in two species of woodland salamander, *Plethodon glutinosus* and *P. cinereus,* dosed at a range of 2.24 to 8.97 kg/ha of a 25% wettable powder malathion formulation. There was a

significant inhibition of cholinesterase in *P. glutinosus* at 5.6 kg/ha but not at 2.24 kg/ha. No effects on cholinesterase were noted at *P. cinereus* at any test concentration (Baker, 1985).

3.2.5 Aquatic Invertebrate Toxicity

Malathion is moderately to very highly toxic to most aquatic invertebrates on an acute basis, depending on the sensitivity of the species. The median lethal concentration of malathion ranges from 0.5 µg/L in the scud (Mayer and Ellersieck, 1986) to greater than 130 mg/L in freshwater snails and mussels (Keller and Ruessler, 1997; Tchounwou et al., 1991) (figure 3–2; appendix B-2). Amphipods and cladocerans are the most sensitive group of aquatic invertebrates. Aquatic insect toxicity ranges from 0.69 µg/L for the stonefly nymph, to 385 µg/L in snipe fly larvae (Mayer and Ellersieck, 1986).

Snell and Persoone (1989) reported 24-hour NOEC values of 11.4 and 22.9 mg/L for the rotifers, *Brachionus plicatilis* and *B. rubens*, respectively. Desi et al. (1976) showed reduced shell closing activity for a freshwater mussel, *Andonta cygnea*, during a 48-hour exposure to malathion at 10,000 µg/L, and no change was noted at 1,000 µg/L or less. In a 7-day static test using *Daphnia magna*, the reported NOEC was 1.0 µg/L (Desi et al., 1976). Reported NOEC values for the midge *Chironomus tentans*, based on mortality and AChE activity, were 320 and 0.26 µg/L, based on 9-day and 24-hour exposures. Relyea (2005) reported NOEC values of 320 µg/L, based on effects on dragonfly and giant water bug populations after dosing with malathion. In a 21-day continuous exposure study using *D. magna*, the reported NOEC was 0.06 µg/L, while the reported LOEC was 0.10 µg/L (USEPA, 2006a).

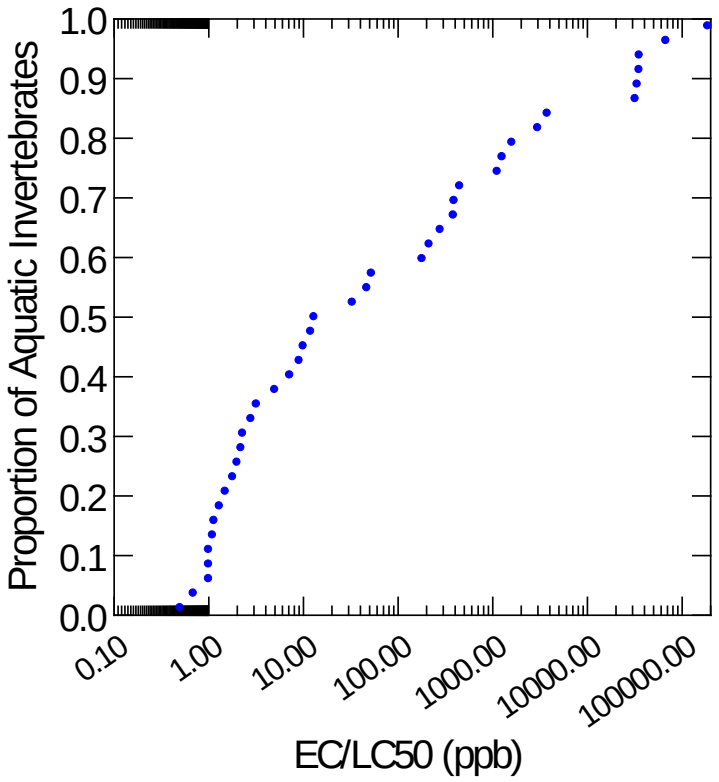

Figure 3–2. Acute aquatic invertebrate toxicity distribution for malathion

3.2.6 Aquatic Plant Toxicity

Based on a review of the literature and available databases, such as ECOTOX, the green algae *Pseudokirchneriella subcapitata* is the most sensitive aquatic plant with a reported median effective concentration EC_{50} of 2,040 µg/L and a corresponding NOEC of 500 ppb (Yeh and Chen, 2006). The most tolerant species is the blue green algae *Nostoc calcicola*, with a NOEC of 200,000 ppb and no reported EC_{50} value (Piri and Ordog, 1999). Premazzi (1984) provides summaries of two studies where phytoplankton dosed at 1 mg/L of malathion had a 7% decrease on C^{14} fixation; however, no other effects were reported, and it is unknown whether the decrease was statistically significant. Moore (1970) reported a NOEC of 1.45 mg/L based on percent inhibition of growth in *Euglena gracilis*. Studies with malathion and the aquatic macrophyte *Spirodela polyrhiza* (large duckweed) report a NOEC of 24,065 µg/L (Whothley and Schott, 1973, as cited in US FS, 2008). Tagatz et al. (1974) reported no effects to *Juncus* spp. (rush) after applications of ULV malathion at 57 g/ha applied 3 times biweekly. Based on the lack of toxicity to terrestrial plants at rates much higher than those proposed in the program, toxic effects to aquatic plants would not be expected to occur from applications of malathion.

3.2.7 Formulation and Metabolite Aquatic Toxicity

Several formulation-related studies have been conducted using malathion; however, little data appears to be available for the formulation proposed for use in the fruit fly program (table 3-2). Based on the available data for other formulations of malathion, sublethal and lethal acute toxicity appears to be within the range reported for aquatic studies conducted using the technical material.

Several metabolites of malathion can occur in aquatic environments. USEPA (2006) provides a summary of a study where the fathead minnow was used to determine the relative toxicity of several known and proposed hydrolytic metabolites of malathion. Using the fathead minnow 96-hour LC_{50} (8.65 mg/L), this value was compared to the threshold level value (TLm) for each of the metabolites (table 3-3).

With the exception of diethyl fumarate and maleic acid, all metabolites were less toxic to the fathead minnow when compared to malathion. Confidence intervals were not presented but, based on the similarity of the malathion, diethyl fumarate, and maleic acid values, they are not expected to be statistically significant from the parent toxicity value. Bender and Westman (1978) conducted 96-hour LC_{50} studies using the eastern mudminnow, *Umbra pygmaea,* to test the acute toxicity of malathion, diethyl fumarate, dimethyl-phosphorodithioic acid, 2-mercaptodiethyl succinate, and dimethylphosphorothionic acid. Results from the study demonstrated the parent compound to be the most toxic with reported LC_{50} values of 0.24, 8.50, 17.00, 47.00, and 26.04 mg/L, respectively.

Another metabolite that can form in aquatic systems is malaoxon. Available aquatic toxicity data show that malaoxon is approximately 1.5 to 6 times more toxic to fish and 1.8 to 93 times more toxic to amphibians (table 3-4). The conversion of malathion to malaoxon in aquatic environments can range from approximately 1.8 to 10% (CDPR, 1993; Bavcon et al., 2005; USEPA, 2012). Limited data exists regarding malaoxon toxicity to aquatic invertebrates. The estimated 24-hour EC_{50} malaoxon value for *C. tentans* is 5.4 µg/L. Similar exposures using *Chironomus sp.* and malathion (1.9 to 4.12 µg/L) suggest similar or slightly less toxicity than the parent when compared to malaoxon (USEPA, 2012). This comparison has some uncertainty because it is based on one test species and multiple studies where the exact methods are unknown. It is assumed that malaoxon is most likely more toxic to aquatic invertebrates than the parent; however, due to its low percentage of occurrence in aquatic systems and its rapid breakdown, it is not anticipated to pose a greater aquatic risk when compared to malathion.

Table 3-2. Malathion Aquatic Toxicity Values for the Typical End Use Product.

Test Organism	Length/Endpoint	% AI	Toxicity Value (µg/L)	Reference
Rainbow trout	7–10 d 25% reduction in brain AChE	55 EC	175	Post and Leasure, 1974
Brook trout	7–10 d 25% reduction in brain AChE	55 EC	120	Post and Leasure, 1974
Coho salmon	7–10 d 25% reduction in brain AChE	55 EC	300	Post and Leasure, 1974
Chinook salmon	96-hour LC_{50}	500 EC	120	Parkhurst and Johnson, 1955
Sheepshead minnow	96-hour LC_{50}	57 EC	55	USEPA, 2006
Bluegill sunfish	96-hour LC_{50}	57 EC	25	Pickering et al., 1962
Fathead minnow	96-hour LC_{50}	57 EC	190	Pickering et al., 1962
Mummichog, *Fundulus heteroclitus*	96-hour EC_{50}	50 EC	22.51	Trim, 1987
Daphnia magna	48-hour EC_{50}	25 NR	3.0	Rassoulzadegan and Akyurtlakli, 2002
Daphnia magna	48-hour EC_{50}	57 EC	2.2	USEPA, 2006
Culex fatigens	48-hour EC_{50}	57 EC	450	Azmi et al., 1998
Eastern Oyster, *Crassostrea virginica*	96-hour EC_{50}	57 EC	2,960	USEPA, 2006
Anisops sardeus	48-hour LC_{50}	NR^{+}	42.2	Lahr et al., 2001
Fairy shrimp, *Streptocephalus sudanicus*	48-hour LC_{50}	NR^{+}	67,750	Lahr et al., 2001

EC = Emulsifiable Concentrate; NR = Not reported; NR^{+} = Percent a.i. not reported but a Fyfanon formulation was tested.

Table 3-3. Toxicity of Hydrolytic Metabolites of Malathion to the Fathead Minnow.

Metabolite	**96-hour TLm (mg/L)**
Dimethylphosphorodithioic acid	23.5
Diethyl fumarate	4.5
2-mecaptodiethyl succinate	35.0
Dimethylphosphorothionic acid	42.5
Maleic acid	5.0
Diethyl maleate	18.0
Dimethyl phosphate	18.0
Thioglycolic acid	30.0
Dimethyl phosphate	225.0
Diethyl succinate	140.0
Diethyl dl-tartarate	650.0
Bis(hydroxymethyl) phosphinic acid	29.0
Ethylene phosphate	34.0

Table 3–4. Malaoxon Toxicity to Aquatic Organisms

Test Organism	**Endpoint/ Length**	**Toxicity Value (**µg/L)	**Malathion Value (µg/L)**	**Reference**
Common carp, *Cyprinus carpio*	48-hour LC_{50}	1600	2,100	USEPA, 2012
Killifish, *Oryzias latipes*	48-hour LC_{50}	280	1,800	Tsuda et al., 1997
African clawed frog, *Xenopus laevis*	96-hour EC_{50}	180	330	Snawder and Chambers, 1989
Foothill yellow-legged frog, *Rana boylii*	96-hour LC_{50}	2.3	2,137	Sparling and Fellers, 2007

Midge, *Chironomus riparius*	24-hour EC_{50}	5.4	NA	USEPA, 2012

4.0 EXPOSURE ASSESSMENT

4.1 Human Health Exposure Assessment

The exposure assessment estimates the potential exposure of humans to malathion. Beginning with the use and application method for malathion, a complete exposure pathway then includes (1) release from a malathion source, (2) an exposure point where contact can occur, and (3) an exposure route such as ingestion, inhalation, or dermal. In this way, we identify the potentially exposed human populations and complete exposure pathways, and then qualitatively or quantitatively evaluate exposure for the identified human populations.

4.1.1 Identification of Potentially Exposed Human Populations and Complete Exposure Pathways

Based on the broadcast treatments of a malathion bait spray by ground or air, workers in the program are the most likely human population segment to be exposed to malathion. Occupational exposure to malathion may occur through inhalation and dermal contact during ground and aerial applications. Direct contact exposure from the application of a malathion bait spray will be minimal if workers adhere to label requirements (Loveland Products, Inc., 2015) with the use of personal protective equipment (PPE), general safety hygiene practices, and restricted entry intervals into treated areas after application. The label required PPE includes long sleeved shirt and long pants, shoes plus socks, and protective gloves (chemical resistant gloves made of barrier laminate or butyl rubber, nitrile rubber, or viton >14 mils). The safety datasheet (Loveland Products, Inc., 2016) also recommends goggles or shielded safety glasses for eye protection, and suitable respiratory equipment in case of inadequate ventilation or risk of inhalation of mists or vapors. The occupational exposure limits (8 hour time weighted average) for malathion are 15 mg/m^3 (total dust, skin) (the Occupational Safety and Health Administration permissible exposure limit) and 1 mg/m^3 (inhalable fraction and vapor) (the American Conference of Governmental Industrial Hygienists threshold limit value). Off-site drift of malathion bait spray applications may occur, but will be reduced by adherence to the label requirement of a large droplet size (4–6 mm) (California Department of Pesticide Regulation, 2017; Florida Department of Agriculture and Consumer Services, 2015). A study of a simulated backpack application (1% suspension of a malathion protein bait) used in the control of Mediterranean fruit flies in South Australia indicated that there is little potential for airborne exposure. Malathion was not detected in any air samples from workers applying malathion bait spray, although malathion was detected on PPEs such as overalls, gloves, and hats (Edwards et al., 2007). Accidental exposure to malathion may occur for a worker during mixing, loading, and application. Dermal contact is the main exposure route during an accidental exposure. This accidental exposure scenario for dermal contact is further quantified in the next section (4.1.2).

The public, including nearby residents, are not recognized as a potentially exposed population group due to label requirements and program standard operating procedures to minimize exposure. First, APHIS uses malathion bait spray treatments only in commercial and ornamental plantings (California Department of Pesticide Regulation, 2017; Florida Department of Agriculture and Consumer Services, 2015). Second, the public receives advanced notification

about exotic fruit fly eradication activities, which allows them to avoid exposure by not being in the area when activities occur. Third, the label has restricted re-entry intervals into treated areas that would reduce exposure to the public. Dietary exposure will be low due to the rapid degradation of malathion on treated commodities and the label required post-harvest intervals.

There is no complete exposure pathway through groundwater because of the low potential for the small amount of malathion applied to the foliage to be released into soil. Malathion that comes into contact with soil may be mobile however it will it will degrade quickly, and is unlikely to leach into groundwater (see Section 2.3).

There is no complete exposure pathway identified for surface waters as a drinking source. Drift and runoff are not expected to be significant from program applications of malathion bait spray based on program and label requirements designed to protect surface waters.

4.1.2 Exposure Evaluation

This section quantitatively evaluates accidental dermal exposure to workers. Fruit fly malathion treatments do not occur in the same time and location each year. The duration for a typical eradication is normally two to three months. The application rate for a malathion fruit fly bait spray is 0.18 lb a.i./acre.

Accidental exposure from dermal contact may occur for workers during mixing and loading if gloves are broken; this accidental dermal exposure can be quantitatively evaluated. The unit exposure of the dermal exposure route for the mixing and loading liquids exposure scenario with single layer, and no gloves PPE level (USEPA 2016e) was used to quantify accidental dermal exposure. As detailed in Appendix A, the assumptions used in this exposure scenario lead to estimated exposure doses of 0.063 mg/kg/day and 0.083 mg/kg/day.

4.2 Ecological Exposure Assessment

4.2.1 Terrestrial Exposure Assessment

Exposure levels on vegetation and other forage items for terrestrial non-target vertebrate organisms were calculated using the Terrestrial Residue Exposure Model (T-REX) (USEPA, 2005). T-REX provides an updated version of the Fletcher residue model that was originally based on the Kenaga nomogram used by USEPA/OPP in their risk assessment process for pesticide registration. T-REX allows the user to input variables such as use, application rate/type, percent active ingredient, soil or foliar dissipation half-life, application interval, and number of applications to calculate exposure concentrations on a variety of food items (table 4-1).

Table 4-1. Expected malathion residues (ppm) on selected terrestrial food items using T-REX.

Food Items	Malathion
Upper Bound Estimate	
Short Grass	93.08
Tall Grass	42.66
Broadleaf Plants/Small Insects	52.36
Fruits/Pods/Seeds/Large Insects	5.82

For foliar sprays, the estimates of exposure are based on field collected residue data for several pesticide classes to calculate residue levels for a wide variety of food items. Minimum and maximum residue levels were calculated for each food item (Hoerger and Kenaga, 1972). The model was updated by Fletcher to account for any potential differences in new chemistry classes that had been developed after Kenaga (Fletcher et al., 1994). Based on over 200 residue studies, the model was shown to provide an accurate representation of residues for certain food items, but in some cases such as long grass, it overestimated residues. The current T-REX model provides daily residue values as a mean and upper bound estimate. All exposure values in this risk assessment are based on the upper bound residue estimates. In addition to the calculated residue data, the T-REX model allows the user to input toxicity endpoints that can be compared to exposure values to determine if exposure levels exceed benchmark effect levels.

The T-REX model does not provide exposure estimates for residues based on any potential reduction that would be seen from the implementation of application buffer zones. The exposure values that T-REX calculates are those that would result from a direct application to the food item of interest.

4.2.2 Aquatic Exposure Assessment

Aquatic residues for malathion that may occur as a result of runoff and drift were estimated using available drift and environmental fate models. Drift estimates were made using the AgDrift model to determine the potential for off-site transport from drift. AgDrift is a pesticide drift deposition model that provide site- and application-specific information as input to determine application efficiency and off-site drift residues. AgDrift was developed from AgDisp which is a model which is a model that was developed by the USDA Forest Service beginning in the early 1980's, and served as the platform for the development of the AgDrift model which has become a regulatory tool for the USEPA/OPP in the registration of pesticides (Hewitt et al., 2002; Teske and Curbishley, 2003). Both models have a tiered approach that allows the user to choose default values or provide more specific data, based on the available information. Both models have been validated under various application scenarios in the literature (Duan et al., 1992a; Duan et al., 1992b; Teske et al., 2000; Teske and Thistle, 2004). In general, aerial application predictions slightly underestimate drift within the first 80 m, but over predict at increasing distances by a

factor of two to four at distances up to approximately 300 m (Duan et al., 1992a,b; Bird et al., 2002; Teske and Thistle, 2003; Thistle et al, 2008).

The proposed droplet size in the fruit fly program (4–8 mm) is more than ten times greater than the largest median droplet size that can be selected in AgDrift. AgDrift aerial applications allow for a 521.38 µm median droplet size as a maximum (American Society of Agriculture Engineers (ASAE) very coarse to extremely coarse), while ground applications allow for a maximum 439.39 µm median droplet size (ASAE coarse to very coarse). Estimates of drift using AgDrift are very conservative in this analysis due to the limitations of the model to assess a larger droplet size. A larger droplet size will reduce the amount of pesticide that can drift off site. Drift scenarios modeled in AgDrift used default settings other than selection of droplet size spectrum.

Application efficiency and drift values from ground and aerial applications using AgDrift were entered into the USEPA/OPP pesticide aquatic fate model, Pesticide Water Calculator (PWC). The PWC allows the user to input pesticide-specific chemistry and environmental fate data and then select crop- and weather-specific information that can be used to generate aquatic residues in water and sediment. The crop scenario selected was a California citrus crop with three applications of 0.18 lb a.i./ac occurring three times on 6-day intervals. Residues for each water body are reported as 90th percentile values based on weather data for the selected scenario in California. Residues were estimated using USEPA default field area and water body volume values for the pond and reservoir scenarios. In addition, a wetland habitat was modeled using the PWC custom water body size and was assumed to be a static, shallow water body. The custom water body modeled had an area of 12 m^2 and a depth of 0.3 m to represent a small isolated wetland habitat. Residues were estimated at peak and varying time periods to represent acute and chronic exposures that can be compared to available toxicity data (table 4-2).

Table 4-2. PWC estimated malathion residues (µg/L) in various water body types using ground and aerial applications for California citrus.

Application method/ Water body	**Peak**	**4-day**	**21-day**	**60-day**
Ground/ Pond	9.06	4.02	2.12	0.98
Ground/Reservoir	21.30	9.48	2.41	1.24
Ground/Wetland	492.0	213.0	48.5	21.1
Aerial/Pond	12.80	5.62	3.47	1.40
Aerial/Reservoir	21.10	9.43	2.74	1.55
Aerial/Wetland	489.0	212.0	49.8	23.7

These estimates are considered conservative because the contribution from drift, which ranges from approximately 25 to greater than 60% depending on the application method, is not reflective of actual drift as a result of the limitations in the droplet size selection for the drift model. As previously stated, the droplet sizes used in the program are approximately ten fold greater than the largest median droplet size that can be selected using AgDrift, and because a

larger droplet size reduces drift, the amount of drift may be overestimated by the model. Also, the estimated malathion residues do not account for any buffers that may be applied to aquatic water bodies.

5.0 RISK CHARACTERIZATION

Risks associated with potential adverse effects are characterized qualitatively and quantitatively in this section. Results from the risk characterization suggests that the use of malathion bait spray for the fruit fly eradication program will pose minimal risks to human health for all population segments, and ecological risks would be negligible or incidental and localized.

5.1 Human Health

The risk to workers exposed to malathion via oral, inhalation, and dermal routes during applications is minimized by the use of PPE and adherence to other label requirements such as restricted re-entry intervals into treated areas. Malathion is a hazard to humans because of its ability to inhibit AChE through oral, inhalation, and dermal exposure. The low potential for significant exposure from the program use of a malathion bait spray suggests there are minimal risks to workers.

The risk to the public from malathion exposure is minimal because the program will only make applications in commercial and ornamental nurseries, the public is notified in advance of the treatment, and label-required restricted entry intervals are observed. Dietary risk is also low due to the short half-life of malathion on any treated commodities and label required post-harvest intervals. Risk to drinking water is also very low based on estimated aquatic residues that were determined for aquatic resources.

The risks associated with accidental dermal contact exposure to workers during mixing and loading are estimated using hazard quotients (HQs) calculated from the USEPA risk estimation equation for non-carcinogens:

HQ = Exposure Dose / Reference Dose

Table 5-1 summarizes the results for the accidental direct contact exposures. The acute reference dose of 0.1 mg/kg/d is the appropriate toxicity value because an accidental exposure is considered an infrequent occurrence.

Table 5-1. Risk Summary Associated with an Accidental Exposure for a Worker.

Exposure Scenario		**Exposure Dose (mg/kg/day)**	**Reference Dose (mg/kg/day)**	**Hazard Quotient**
Dermal exposure route during mixing and loading liquids	Central	0.063	0.1	0.6
	Upper	0.083	0.1	0.8

HQ values that exceed 1.0 suggest that there may be risk to a specific group of the population, while values below 1.0 suggest that risk is minimal. The results summarized in table 5-1 show that all the hazard quotients associated with accidental dermal exposure are below 1.0 for workers. Detailed calculations are included in appendix A.

5.2 Terrestrial and Aquatic Risk Characterization

5.2.1 Terrestrial Risk Characterization

5.2.1.1 Direct and Indirect Risk to Mammals

The most sensitive toxicity endpoints were used as a basis to determine direct acute and chronic risk to mammals. Instead of using the lowest reported LD_{50} value as an effects endpoint, the acute rat neurotoxicity NOEL (1,000 mg/kg) was used to provide a conservative estimate of risk. The LOEL for the study was based on statistically significant cholinesterase inhibition. The chronic endpoint used in the risk characterization was based on the lowest reported reproductive NOEL (25 mg/kg/day) from a cholinesterase inhibition study. Adjusted acute and chronic NOEL values were calculated for different sized mammals that are herbivores, insectivores, and granivores (table 5-2).

Table 5-2. Different mammal class parameters used to calculate adjusted acute and chronic NOEL values.

Mammalian Class	Body Weight (g)	Ingestion (dry) (g bwt/day)	Ingestion (wet) (g/day)	% body wgt consumed	(kg-diet/day)	Adjusted Acute NOEL	Adjusted Chronic NOEL
Herbivores/	15	3	14	95	1.43E-02	2197.83	54.95
Insectivores	35	5	23	66	2.31E-02	1778.28	44.46
	1000	31	153	15	1.53E-01	769.16	19.23
Granivores	15	3	3	21	3.18E-03	2197.83	54.95
	35	5	5	15	5.13E-03	1778.28	44.46
	1000	31	34	3	3.40E-02	769.16	19.23

All acute risk quotient values were at or below 0.04 suggesting low acute risk to wild mammals based on the acute NOEL (table 5-3). Chronic risk quotient values ranged from 0.10 to 1.62 suggesting chronic risk for certain mammal groups that feed within treated areas.

Table 5-3. Calculated mammalian risk quotient values for malathion use in the fruit fly program.

Dose-based RQs (Dose-based EEC/ NOEL)	15 g mammal		35 g mammal		1000 g mammal	
	Acute	Chronic	Acute	Chronic	Acute	Chronic
Short Grass	0.04	1.62	0.03	1.38	0.02	0.74
Tall Grass	0.02	0.74	0.02	0.63	0.01	0.34
Broadleaf plants/small insects	0.02	0.91	0.02	0.78	0.01	0.42
Fruits/pods/large insects	0.00	0.10	0.00	0.09	0.00	0.05
Seeds (granivore)	0.02	0.63	0.01	0.54	0.01	0.29

*Values are less than 0.001

Chronic risk quotients exceeding one assume that there is some risk because the exposure concentrations exceed the effect thresholds. However, the chronic risk estimates in this assessment are conservative based on multiple assumptions. The effects data point was based on cholinesterase inhibition and does not imply a sublethal effect that could affect survival. In addition, the NOEL was based on a concentration that was given as a daily dose in a long term study. This type of situation would not occur with program malathion applications because of the short time of application, and residues that would not persist due to the rapid breakdown of the parent and other toxic metabolites, such as malaoxon. The above risk characterization also assumes that wild mammals would feed exclusively on treated food items. Malathion treatments will occur in commercial nurseries using a large droplet size that includes a fruit fly attractant. The use of a larger droplet reduces coverage within a treatment area with applications directed at host plants.

Direct acute and chronic risk of malathion to mammals is expected to be minimal from ground or aerial malathion applications in commercial nurseries. Habitat loss from phytotoxic effects of malathion to terrestrial plants is not expected because of the low reported toxicity of malathion to plants. Doses at which effects have been seen are well above those that could occur from program applications. Indirect risks from loss of plant material that could serve as a food source for some mammals would also be low because of the low phytotoxicity of malathion. The other possible indirect effect that should be considered is loss of invertebrate prey for those mammals that depend on insects and other invertebrates as a food source. Malathion has a wide variety of sensitivities to insects; however, a complete loss of invertebrates from a treated area is not expected because of low program rates and application techniques.

Limited field studies are available that address the indirect impacts of malathion applications to small mammals. McEwen et al. (1996) found no post-treatment effects on deer mouse populations in North Dakota after grasshopper-related malathion applications. Erwin and Sharpe (1973) assessed the impacts of malathion ULV applications at program rates and saw no effects on small mammal populations in Nebraska. In another field study, chipmunk populations were reduced 30 to 55% after treatment with 2 lb a.i/ac of malathion, which is more than eleven times the maximum amount allowed in the program.

5.2.1.2 Direct and Indirect Risk to Birds

The lowest reported avian LD_{50} value (167 mg/kg) was used to generate adjusted acute values for bird body weights ranging from 20 to 1,000 g (table 5-4). The adjusted values ranged from 85.39 to 153.5 mg/kg.

Table 5-4. Adjusted toxicity value (LD_{50}) for different avian class sizes.

Avian Class	Body Weight (g)	Ingestion (dry) (g bw/day)	Ingestion (wet) (g/day)	% body wgt consumed	(kg-diet/day)	Adjusted LD_{50} (mg/kg-bw)
Small	20	5	23	114	2.28E-02	85.39
Mid	100	13	65	65	6.49E-02	108.71
Large	1000	58	291	29	2.91E-01	153.55

Based on the adjusted toxicity values and upper bound exposure estimates expected from a full application of malathion with no use of an application buffer zone, the acute risk quotient values ranged from 0.01 to 1.24 (table 5-5).

Table 5-5. Acute risk quotient values for malathion based on the lowest acute LD_{50} and assuming no application buffer zone.

Dose-based RQs	Avian Acute RQs		
(Dose-based EEC/adjusted LD_{50})	20 g	100 g	1000 g
Short Grass	1.24	0.56	0.18
Tall Grass	0.57	0.25	0.08
Broadleaf plants/small insects	0.70	0.31	0.10
Fruits/pods/seeds/large insects	0.08	0.03	0.01

Using the lowest reported LC_{50} value (2,639 mg/L) and the lowest chronic reproductive NOEC (110 mg/L), acute and chronic dietary risk quotient values were below 1 (table 5-6). These risk quotient values are based on the maximum application rate for malathion with no application buffer zone, use of upper bound estimates of residues, and the assumption that birds would feed exclusively on malathion treated food items.

Based on the assessment above, direct avian acute and chronic risk is expected to be minimal. The assessment is conservative because the residues are based on upper bound estimates, assume that all affected birds will feed exclusively on one type of food item, and that all of the food they consume has maximum malathion residues. Malathion degrades quickly in the environment and residues on food items are not expected to persist.

Table 5-6. Acute and chronic risk quotient values for birds based on the lowest dietary acute and chronic toxicity values.

Dietary-based RQs (Dietary-based EEC/LC_{50} or NOEC)	RQs	
	Acute	**Chronic**
Short Grass	0.04	0.85
Tall Grass	0.02	0.39
Broadleaf plants/small Insects	0.02	0.48
Fruits/pods/seeds/large insects	0.00*	0.05

*Values are less than 0.001

Possible indirect risks to birds are expected to be minimal based on the discussion of indirect risks to mammals from malathion applications. Malathion has low toxicity to plants and impacts to terrestrial invertebrates are anticipated to be the greatest within the spray blocks of commercial operations. Birds typically have a larger foraging area than the areas that would be treated with malathion and not all invertebrates within a treatment block would be impacted based on the range of sensitivities to malathion and the method of application using a large droplet size.

The possible indirect effects of malathion applications to birds have been evaluated in several field studies that evaluated impacts at higher application rates than those proposed in the fruit fly eradication program. A 3-year study was conducted to determine the indirect effects of malathion on survival and growth of Brewer's sparrows (*Spizella breweri*) and sage thrasher (*Oreoscoptes montanus*) nestlings in Idaho (Howe, 1993; Howe et al., 1996). Although the total invertebrate availability was reduced by standard malathion spray applications (0.5 lb a.i./ac), nesting birds were shown to switch their diets to the remaining insects and reproduce as successfully as birds on untreated control plots. Adults had to forage longer on treated plots, and nestlings demonstrated an increased propensity for parasitic blowfly infestations. Either of these indirect effects might impact survival in some situations. However, this particular field study did not show these effects to be significant.

George et al. (1995) evaluated the effects of grasshopper malathion applications on vesper sparrow, *Pooecetes gramineus*, and horned lark, *Eremophila alpestris*, densities in Colorado, Idaho, North Dakota, Utah, and Wyoming, and found no effect 10- and 21-days post treatment. In a summary of a study conducted in Colorado, Dinkins et al. (2002) reported no effect on horned lark pair densities when comparing fields that had been treated with 0.6 kg/ha of malathion to untreated areas. Norelius and Lockwood (1999) evaluated several different grasshopper insecticides and their potential effects on bird densities. Applications were made using alternating swath treatments within a spray block for all pesticides with the exception of fipronil. No negative effects on bird density were noted in the malathion-treated blocks.

Pascual (1994) found no effects on the nesting and reproductive success of the blue tit, *Parus caeruleus*, after a forestry application of a ULV malathion formulation at a rate of 1.16 kg a.i./ha

or 1.03 lb a.i./ac. Although there was a reduction in some lepidopteran species, others were unaffected. None of the breeding parameters (nest abandonment, nest success, hatching success, nestling mortality, daily survival rate, and nestling weight) were affected when compared to control plots.

5.2.1.3 Direct and Indirect Risk to Amphibians and Reptiles

Risk to amphibians was evaluated using the available acute and chronic toxicity data as well as fish data that can be used as a surrogate for estimating risk to amphibians. In the case of malathion, the available toxicity data demonstrates that fish species are more sensitive than amphibians. The available acute effects data shows a range of amphibian toxicity values for several species of frog tadpoles ranging from 0.56 to 13.27 mg/L. Expected aquatic residues from malathion applications in wetland habitats where amphibians would be more prevalent were approximately 212 to 213 µg/L, while pond residues ranged from 4 to 5.62 µg/L as 4-day averages. While these values are below expected effect threshold values, some sensitive individuals could be at risk. The risk is expected to be low based on the conservative assumptions in the drift and runoff modeling that were previously discussed. Sublethal effects such as developmental delays, reduced food consumption and body weight, and teratogenesis have been observed at concentrations above 0.5 mg/L in short and long term studies. Observed sublethal impacts occur at concentrations approximately twice those estimated in this assessment, suggesting a low probability of sublethal risk from malathion exposure to amphibians. Indirect risk to amphibians through the loss of prey items in aquatic habitats may occur based on the risk of malathion to some aquatic invertebrates and vertebrates. These risks will be reduced by the method of application and adherence to label requirements to avoid aquatic water bodies. Adult amphibians that may forage for terrestrial invertebrates away from aquatic breeding sites could also be at risk from the loss of prey items, but these risks will be reduced by the method of malathion application in the fruit fly program.

For reptiles, available toxicity data using malathion suggests that no lethal or sublethal impacts would be anticipated. However, the effects data for reptiles is limited; thus, the results from the avian risk characterization can be used to approximate the potential for risk. Reptiles that forage exclusively in commercial nurseries where treatments may occur are at greater risk from direct toxicity of consuming contaminated prey. This can include plant material and invertebrates. Indirect risk may also occur within a spray block due to loss of invertebrate prey as a result of fruit fly applications. Invertebrate impacts will be reduced with the use of a large droplet size that contains a fruit fly attractant that would be more specific to the target pest. Some sensitive invertebrates would be impacted; however, the range of species sensitivities and the low use rates in the program are not expected to result in widespread impacts to invertebrate populations that would occur in commercial nurseries. Many reptiles are general foragers and invertebrates that are not impacted by malathion treatments would be available as prey.

5.2.1.4 Risk to Terrestrial Invertebrates

The risks to terrestrial invertebrates will be greatest for those invertebrates within the treatment block and may be attracted to the fruit fly attractant. The risk to off-site terrestrial invertebrates is reduced by the implementation of application buffers, where applicable, and other measures to reduce off-site drift. The fruit fly program uses a larger droplet size (4–8 mm) that will significantly reduce the probability of off-site drift during application. Sensitive terrestrial invertebrates would be impacted within the treatment area; however, these are managed areas that are highly disturbed from other management activities. The use of a large droplet with an attractant allows for lower use rates that would reduce risk to terrestrial invertebrates within the spray block. The potential for long term exposure and effects to terrestrial invertebrates decreases quickly because the residual toxicity of malathion is approximately four days.

5.2.1.5 Direct and Indirect Risk to Terrestrial Plants

Available malathion effects data for terrestrial plants demonstrates low toxicity, and along with the low exposure levels, suggests low direct risk to listed terrestrial plants. There is the potential for indirect effects to listed plants from impacts to terrestrial invertebrate pollinator populations that may be decreased by malathion treatments. Malathion is a broad spectrum insecticide that can impact a variety of insect taxa. Impacts to pollinators can be significant because of available toxicity data for honey bees that demonstrates high contact toxicity from malathion exposures. Residual toxicity studies on foliage demonstrate a NOEL of less than 1.6 lb a.i./acre, which is an approximately ten-fold higher application rate than is used in the fruit fly program (USEPA, 2012). Risk to pollinators is reduced because of the short residual toxicity of malathion and the use of a large droplet size containing an attractant for fruit flies.

5.2.2 Aquatic Risk Characterization

Available acute and chronic effects data for malathion and fish were within the range of estimated aquatic concentrations for ground and aerial applications (figure 5-1). Examples of endpoints evaluated in both short- and long-term studies consisted of reproductive parameters, cholinesterase inhibition, swimming behavior, skeletal malformations, and eye diameter. The range of available toxicity data above the estimated exposure values suggests that direct acute and chronic effects to listed fish from malathion could occur for sensitive species. Consumption of contaminated prey is not expected to be a significant pathway of exposure for aquatic species based on expected residues and the low bioconcentration factor value.

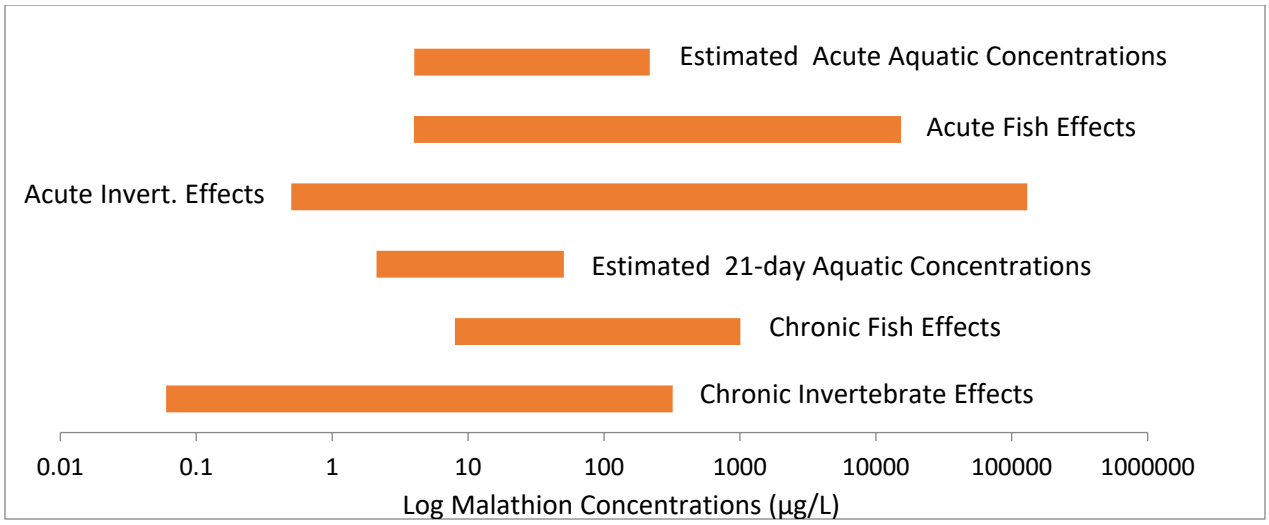

Figure 5-1. Malathion risk characterization for fish and aquatic invertebrates.

To address indirect risk of malathion applications to fish habitat, estimated residues were compared to the lowest available aquatic plant toxicity value. Toxicity to plants, including algae, could result in indirect effects to habitat and food for fish and aquatic invertebrates. Using the lowest reported laboratory NOEC value, the benchmark effects level for aquatic plants was 500 µg/L, which is well above the estimated environmental concentration from aerial and ground applications of malathion. Estimated residues were two to ten times below the aquatic plant NOEC for both aerial and ground applications. Therefore, indirect effects to fish from impacts of malathion applications to aquatic plants are not expected.

The other area of potential indirect effects is the impact of malathion on prey items used by aquatic species. Comparison of available acute fish and aquatic invertebrate toxicity distribution data to the residues estimated from ground and aerial malathion applications demonstrates risk to some sensitive species.

5.2.1.1 Aquatic Field Studies Regarding Fish and Aquatic Invertebrates

The USEPA (2006a) provides a review of two field studies in which multiple malathion applications were made over water for mosquito control, and effects to fish were monitored in estuarine environments. Mortality and AChE inhibition were noted in both studies; however, these results have limited use in assessing risk from program-related malathion applications because rates were much higher than those proposed in this program. In another USEPA study review, four malathion applications were made to freshwater ponds containing bluegill over an 11-week period. Reductions in bluegill populations were attributed to a loss of aquatic invertebrates at 0.02 and 0.002 mg/L, which is above levels predicted from program activities. In another review, malathion applications were made within 25 feet of a creek in Alabama and monitored for aquatic invertebrate and fish effects over a 3-year period. A slight reduction in AChE was noted in fish collected at the area of application; however, there were no effects on

the population during the study. There were some differences in the abundance of invertebrate taxa, but the authors could not attribute the differences to malathion applications. Relyea and Diecks (2008) observed sublethal impacts to amphibians from the loss of aquatic invertebrates in an outdoor field microcosm study. Dosing occurred weekly for 7 weeks at 10µg/L, with additional doses of 50 and 250 µg/L in some cases. However, dosing levels and frequency of dosing exceed those expected from malathion applications in this program.

6.0 UNCERTAINTIES AND CUMULATIVE IMPACTS

The uncertainties associated with this risk evaluation arise primarily from lack of information about the effects of malathion, its formulation, 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 HHERAs with any environmental stressor. In addition, there is uncertainty in where and how often exotic fruit fly detections may occur within a specific state, and throughout the rest of the United States. There is uncertainty regarding the extent of malathion use during any given infestation because its use is based on site-specific factors.

Another area of uncertainty is the potential for cumulative impacts to human health and the environment including: 1) repeated worker and environmental exposures to malathion from program activities in conjunction with other crop use sources, and 2) co-exposure to other chemicals with a similar mode of action.

Malathion has many commercial agriculture, industrial, and household uses beside governmental uses. The annual use of malathion was approximately 11–13 million pounds in 2000, and approximately 15 million pounds in 2009 (USEPA, 2009). The APHIS fruit fly eradication program use of malathion during limited fruit fly outbreak cases per year is much less compared to the normal agriculture use. Applications of malathion are infrequent and at comparatively low application rates (0.18 lb/ac).

Cumulative impacts may occur from malathion use in relation to other chemicals used in the program 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 or outside the program with the same toxic action may also occur. The other pesticides used in the fruit fly eradication program include spinosad, lambda-cyhalothrin, naled, DDVP, and diazinon. 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. Naled, DDVP, and diazinon are also organophosphate pesticides with the same toxic mode of action. All of the program insecticides have multiple other uses that could occur in areas where fruit fly treatments may occur. The spatial and temporal variability in these other uses relative to treating sporadic exotic fruit fly outbreaks make it difficult to quantify cumulative impacts from the additional use of program insecticides. The results of USEPA's Organophosphorate Cumulative Risk Assessment (2006b) present exposure and risk data from food, water, and residential use to the U.S. population, and support a reasonable certainty of a no harm finding as required by the FQPA. Cumulative impacts from the proposed uses of malathion, naled, and DDVP are expected to be incrementally minor due to the proposed use patterns of these pesticides, adherence to individual pesticide label requirements for risk mitigation measures, and the historical low frequency of positive exotic fruit fly detections. Malathion may have synergistic effects when

used with other organophosphates (US FS, 2008) used in the program. However, these insecticides would not all be used during a given outbreak.

Cumulative impacts from the proposed use of malathion are expected to be incrementally minor due to adherence to individual pesticide label requirements for risk mitigation measures, and the historical low frequency of exotic fruit fly detections in the United States.

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Appendix A
Risk-Estimations for Accidental Occupational Exposure during Mixing and Loading

Parameters and Equations	Units	Exposure Scenario	Mixing and Loading Dermal	Sources
Exposure Dose = PDR/BW	mg/kg-d	Central	6.3E-02	Calculated
		Upper	8.3E-02	
BW=body weight	kg		80	USEPA 2014b
PDR = UE * DMC				
PDR =daily dose rates	mg/day	Central	5.0688	Calculated
		Upper	6.6528	
UE = unit exposure	mg/lb a.i		0.22	The unit exposure of the dermal exposure route for the mixing and loading liquids exposure scenario (single layer, and no gloves PPE level) (USEPA 2016e).
DMC=AR * ATD				
DMC = daily mixing concentration	lb ai/day	Central	23.04	Calculated
		Upper	30.24	Calculated
AR - application rate	lb ai/acre		0.18	Program 24(c) labels
ATD - acres treated per day	acre/day	Central	128	16 acres/hour and 8 hrs day (US FS, 2008)
		Upper	168	21 acres/hour and 8 hrs day (US FS, 2008)
RfD	mg/kg/day		0.1	Acute oral RfD, USEPA 2016b
HQ = Exposure Dose/RfD				
HQ = Hazard Quotient		Central	0.6	Calculated
		Upper	0.8	

Appendix B-1. Malathion acute fish toxicity values

Test Organism	Endpoint/Length	Toxicity Value	Reference
Rainbow trout	96-hour LC_{50}	4.0 µg/L	USEPA, 2006a
Bluegill sunfish	96-hour LC_{50}	20.0 µg/L	USEPA, 2006a
Sheepshead minnow	96-hour LC_{50}	33.0 µg/L	USEPA, 2006a
Red ear sunfish	96-hour LC_{50}	62.0 µg/L	USEPA, 2006a
Walleye	96-hour LC_{50}	64.0 µg/L	USEPA, 2006a
Striped bass	96-hour LC_{50}	60.0 µg/L	USEPA, 2006a
Lake trout	96-hour LC_{50}	76.0 µg/L	USEPA, 2006a
Brown trout	96-hour LC_{50}	101.0 µg/L	USEPA, 2006a
Coho Salmon	96-hour LC_{50}	170.0 µg/L	USEPA, 2006a
Cutthroat trout	96-hour LC_{50}	174.0 µg/L	USEPA, 2006a
Largemouth bass	96-hour LC_{50}	250.0 µg/L	USEPA, 2006a
Yellow perch	96-hour LC_{50}	263.0 µg/L	USEPA, 2006a
Spot	96-hour LC_{50}	320.0 µg/L	USEPA, 2006a
Striped mullet	96-hour LC_{50}	330.0 µg/L	USEPA, 2006a
Green sunfish	96-hour LC_{50}	1,460.0 µg/L	USEPA, 2006a
Tilapia	96-hour LC_{50}	2,000.0 µg/L	USEPA, 2006a
Carp	96-hour LC_{50}	6,590.0 µg/L	USEPA, 2006a
Channel catfish	96-hour LC_{50}	7,620.0 µg/L	USEPA, 2006a
Fathead minnow	96-hour LC_{50}	8,650.0 µg/L	USEPA, 2006a
Goldfish	96-hour LC_{50}	10,700.0 µg/L	USEPA, 2006a
Black bullhead catfish	96-hour LC_{50}	11,700.0 µg/L	USEPA, 2006a
Colorado bonytail	96-hour LC_{50}	15,300.0 µg/L	Beyers, et al., 1994

Appendix B-2. Malathion acute aquatic invertebrate toxicity values

Test Organism	Endpoint/Length	Toxicity Value	Reference
Gammarus fasciatus	96-hour LC_{50}	0.5 µg/L	USEPA, 2006a
Simocephalus serrulatus	96-hour LC_{50}	0.69 µg/L	USEPA, 2006a
Isoperla sp.	96-hour LC_{50}	0.69 µg/L	USEPA, 2006a
Daphnia magna	96-hour LC_{50}	1.0 µg/L	USEPA, 2006a
Pteronarcella badia	96-hour LC_{50}	1.1 µg/L	USEPA, 2006a
Limnephalus sp.	96-hour LC_{50}	1.3 µg/L	USEPA, 2006a
Gammarus lacustris	48-hour EC_{50}	1.8 µg/L	USEPA, 2006a
Daphnia pulex	48-hour EC_{50}	1.8 µg/L	USEPA, 2006a
Neomysis mercedis	96-hour LC_{50}	2.2 µg/L	Brandt et al., 1993
Mysidopsis bahia	96-hour LC_{50}	2.2 µg/L	USEPA, 2006a
Claasenia sabulosa	96-hour LC_{50}	2.8 µg/L	USEPA, 2006a
Hydropsyche sp.	96-hour LC_{50}	5.0 µg/L	USEPA, 2006a
Lestes congener	96-hour LC_{50}	10.0 µg/L	USEPA, 2006a
Paleomenetes kadiankesis	96-hour LC_{50}	12.0 µg/L	USEPA, 2006a
Orconectes nais	96-hour LC_{50}	180.0 µg/L	USEPA, 2006a
Penaeus duorarum	48-hour LC_{50}	180.0 µg/L	USEPA, 2006a
Atherix variegata	96-hour LC_{50}	385 µg/L	USEPA, 2006a
Crassostrea virginica	96-hour LC_{50}	>1,000 µg/L	USEPA, 2006a
Callinectes sapidus	48-hour LC_{50}	>1,000 µg/L	USEPA, 2006a
Asellus brevicaudus	96-hour LC_{50}	3,000 µg/L	USEPA, 2006a
Utterbackia imbecilis	96-hour LC_{50}	40 mg/L	Keller and Ruessler, 1997
Villosa lienosa	96-hour LC_{50}	74 mg/L	Keller and Ruessler, 1997
Villosa villosa	96-hour LC_{50}	180 mg/L	Keller and Ruessler, 1997