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Final Human Health and Ecological Risk Assessment for Malathion Rangeland Grasshopper and Mormon Cricket Suppression 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 the use of the insecticide malathion ultra-low volume (ULV) spray in its cooperative rangeland grasshopper and Mormon cricket suppression program. Malathion is an organophosphate (OP) insecticide. The PPQ proposed end-use product, Fyfanon® ULV AG, is a liquid that can be applied by ground-based equipment or aerially at reduced rates compared to the conventional current labelled rates for grasshopper control.

USDA-APHIS evaluated the potential human health and ecological risks from the proposed use of the Fyfanon® ULV AG insecticide in this assessment and determined that the risks to human health and the environment are low. The proposed use of malathion as an ULV spray with a low volume application rate and adherence to label requirements substantially reduces the potential for exposure to humans and the environment. APHIS does not expect adverse health risks to workers based on low potential for exposure to malathion when applied according to label directions, and use of personal protective equipment during applications. APHIS quantified the potential risks associated with accidental exposure of malathion for workers during mixing, loading, and application based on proposed program uses. The quantitative risk evaluation results indicate no concerns for adverse health risk for program workers from the program application. APHIS treatments are conducted in rural rangeland areas, where agriculture is a primary economic factor with widely scattered single rural dwellings in ranching communities with low population density. The risk to the general public from malathion exposure in the treatment areas from the ground or aerial applications is also expected to be minimal because of the adherence to label requirements and additional program measures designed to reduce exposure to the public.

Malathion risk to non-target fish and wildlife is expected to be low for most groups based on available toxicity data and program controls designed to reduce exposure. The preferred use of reduced agent area treatments (RAATs) and ground and aerial aquatic application buffers reduces exposure for terrestrial and aquatic non-target fish and wildlife. Malathion will impact some sensitive terrestrial invertebrates; however, the low use rates and implementation of RAATs will minimize these impacts.

1.0 INTRODUCTION

USDA-APHIS-PPQ proposes the use of malathion in its rangeland grasshopper and Mormon cricket suppression program. This human health and ecological risk assessment (HHERA) provides a qualitative and quantitative evaluation of the potential risks and hazards to human health, nontarget fish, and wildlife as a result of exposure to the organophosphate (OP) insecticide, malathion. The organophosphates are a group of related pesticides that affect the functioning of the nervous system. The program would apply the insecticide using ultra low volume (ULV) aerial or ground applications to suppress populations of rangeland grasshopper species, such as migratory grasshopper, valley grasshopper, bigheaded grasshopper, clearwinged grasshopper, and Mormon cricket.

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 nontarget fish and wildlife follow USEPA and other published methodologies regarding eco-risk assessments, with an emphasis on those used by USEPA/OPP in the pesticide registration process.

The risk assessment is divided into four sections beginning with the problem formulation (identifying hazard), a toxicity assessment (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 and toxicity assessments to characterize the risk of malathion applications to human health and the environment.

2.0 PROBLEM FORMULATION

Grasshoppers and Mormon crickets are closely related insects that belong to the insect order Orthoptera. Nearly 400 grasshopper species inhabit the 17 western States involved in APHIS' grasshopper program, but only a small percentage are pest species. Anywhere from 15 to 45 species of grasshoppers can be found in a particular rangeland ecosystem, and economic damage can occur when grasshopper populations exceed population thresholds.

Mormon crickets (*Anabrus simplex*) are flightless, shield-backed katydids. Although they do not fly, Mormon crickets are highly mobile and capable of migrating great distances. They move by walking or jumping, and may devour much of the forage in their path.

Both insects damage grasses and other vegetation by consuming plant stems and leaves. Their feeding causes direct damage to plants' growth and seed production, thus reducing valuable livestock forage. The damage they cause to plants may result in soil erosion and degradation, disruption of nutrient cycles, interference with water filtration, and potentially irreversible changes in the flora and fauna of the rangeland ecosystem. In addition, some populations that develop on rangelands can invade adjacent cropland where the value of crop plants is much higher than rangeland grasses (USDA APHIS, 2015a).

Malathion is used to control insects such as aphids, leafhoppers, and Japanese beetles in the agricultural production of a wide variety of food/feed crops (USEPA, 2009). Malathion is also used for mosquito-borne disease control, and is available to home gardeners for residential use on vegetable gardens, home orchards, and ornamentals. APHIS uses malathion against grasshoppers and Mormon crickets when a fast-acting insecticide is needed with very little residual activity. Historically, the grasshopper program commonly used malathion, but has not used the insecticide in recent years (USDA APHIS, 2015b).

Malathion affects the nervous system through acetylcholinesterase (AChE) inhibition. Malathion is converted to its oxon metabolite, malaoxon which is a more potent AChE inhibitor compared to malathion (approximately 22 times as toxic as malathion in mammals) (USEPA, 2016b).

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.

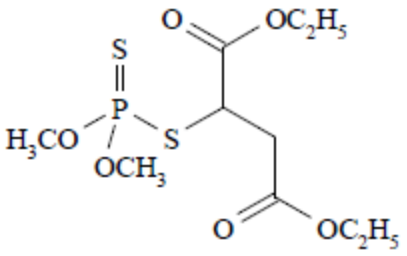

Figure 2-1 The chemical structure of malathion

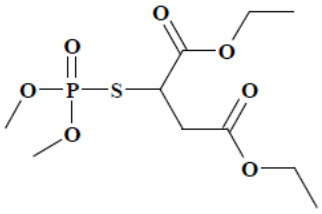

Figure 2-2 The chemical structure of malaoxon

USEPA first registered malathion as an insecticide in 1956. The Program end-use product is Fyfanon® ULV AG (EPA Reg. No. 279-3540, previously 67760-35) contains 96.5% malathion as the active ingredient (a.i.) and 3.5% other ingredients (9.9 pounds malathion per gallon) (FMC, 2017a, Cheminova, Inc., 2012). For grasshopper suppression, the program applies undiluted Fyfanon® ULV AG for ULV spraying at 0.62 lb a.i./acre (conventional) and 0.31 lb a.i./acre (reduced agent area treatments (RAATs)) with approximate total applied volumes of 8 fl oz/acre (conventional) and 4 fl oz/acre (RAATs) by ground or aerial equipment. The program conducts applications in accordance with the Federal Insecticide, Fungicide and Rodenticide Act (FIFRA) Section 3 label for Fyfanon® ULV AG and any applicable FIFRA Section 24(c) Special Local Need labels.

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 (K_{ow}) ranges between 2.29 and 3.30, and the organic carbon normalized partition coefficient (K_{oc}) ranges between 151 (sandy loam) and 308 (sand) (USEPA, 2009, 2016b).

Malaoxon is a 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 its water solubility is 0.5–1.0 g/100 mL (22 ºC) (USEPA, 2016b). Malaoxon has a K_{oc} of 46 L/kg (USEPA, 2009). FMC (2019) reported Koc values ranged from 81 to 327 in guideline studies submitted to USEPA.

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) persistence and degradation, 2) mobility, and migration potential to groundwater and surface water, and 3) plant uptake.

Malathion from ground or aerial applications can be transported into the atmosphere through drift and volatilization as well as fog and wind. The half-life for vapor-phase malathion degradation in air by reaction with photochemically-produced hydroxyl radicals is approximately 5 hours (NIH, 2016). 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. USEPA (2016c) reports biphasic half-lives with the initial half-life less than one day followed by half-lives greater than ten days. Malathion is less persistent in the presence of microbial activity, moisture, and high pH. Inorganic degradation of malathion may be more important in soils that are relatively dry, alkaline, and low in organic content, such as those that predominate in the western program areas. Malathion does not adsorb strongly to soils and is soluble in water. As a result, malathion can be highly mobile and can migrate to surface water via runoff and to groundwater via leaching, particularly if a rainfall occurs soon after application. However, the short persistence of malathion in soil reduces the likelihood of groundwater leaching (USEPA, 2009, 2016b). Leaching is a likely route of dissipation suggested by a lack of malathion residues below 12 inches in the terrestrial field dissipation study. The terrestrial field dissipation data also indicate rapid dissipation with a half-life of less than 2 days (USEPA, 2009). 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 0.5 days in the pH of 7 and 9 solutions, respectively) (USEPA, 2009). Half-lives for aerobic metabolism of malathion in water range from 0.3 to 3.3 d (Walker 1976; Knoch 2001a and Hiler and Mannella 2012 cited in Clemow et al., 2017).

Malathion can break down to many degradates 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 dry soils (USEPA, 2009). The half-life values for malaoxon in soil range from 3–7 days (Paschal and Neville, 1976; US FS, 2008; Bradman et al., 1994). USEPA reported an aerobic soil half-life of 21 days for malaoxon that was used to model environmental concentrations in water (USEPA, 2016b). FMC (2019) provides a summary of additional environmental fate data submitted to USEPA for malaoxon. These data include hydrolysis half-lives of 32.5 days (pH 5), 8.8 days (pH 7), and 6.7 hours (pH 9), aerobic soil metabolism half-lives of 0.2 to 0.6 days, and aerobic aquatic metabolism half-lives of 1 day (North Dokota) and 5.1 days (Georgia), as well as Koc ranging from 1126 (MS silt loam) to 2061 (CA sandy clay loam).

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). The foliar dissipation rates ranged from half-lives of 4.10 to 5.73 d for the non-ULV and ULV applications of malathion, respectively (Moore et al., 2014 cited in Clemow et al., 2017).

Malathion's bioconcentration factors (BCF) are low for fish, ranging from 7.36 in lake trout to 34.4 in willow shiners (Tsuda et al., 1989). The fish BCF values reported by USEPA were 4.2 to 18 (edible), 37 to 204 (viscera), and 23 to 135 (whole fish) (USEPA, 2009). Concerns about bioaccumulation are not anticipated based on the use pattern, low K_{ow}, and lack of bioconcentration in aquatic organisms. Malathion is not expected to bioconcentrate or biomagnify because it is quickly eliminated from fish when moved to clean water (Deka and Mahanta, 2016). Malathion is rapidly metabolized via carboxylesterases with removal of malathion in fish, birds, and mammals with estimated half-lives of 17, 3.44, and 3.32 hour, respectively (Reddy et al. 1989; Cannon et al. 1992, 1993 and Kammerer and Robinson 1994 cited in Clemow et al., 2017).

2.4 Hazard Identification

Malathion is a hazard to human health due to its effects on the nervous system through red blood cell and brain cholinesterase inhibition (because it inhibits AChE enzyme activity essential to the regulation of the human nervous system). Clinical signs of neurotoxicity at relevant doses 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). Organophosphate insecticide cumulative risk assessments (USEPA, 2002; 2006a) show that malathion is a less potent inhibitor of red blood cell cholinesterase and the least potent inhibitor of brain cholinesterase comparing to the other organophosphate pesticides.

2.4.1 Toxic 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. Malaoxon goes through detoxification with subsequent metabolism. Absorption and distribution of malathion and malaoxon are rapid with extensive metabolism and no accumulation in tissues. The available studies indicate red blood cell AChE inhibition is more sensitive to malathion 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 (USEPA, 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 asprostate cancer Hodgkin lymphoma, and soft tissue sarcoma. The HED reviews (USEPA, 2014, 2016d) 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.

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 doses (LD_{50}) in rats are 5,400 mg/kg (males) and 5,700 mg/kg (females) (IV). The acute dermal LD_{50} in rats exceed 2,000 mg/kg for both males and females (III). The acute inhalation median lethal concentration (LC_{50}) in rats exceeds 5.2 mg/L for both males and females (IV). Malathion causes slight eye conjunctival irritation in rabbits that clears in seven days (III), and slight dermal irritation in rabbits (IV). It is not a dermal sensitizer in guinea pigs (USEPA, 2009). Fyfanon® ULV AG contains 96.5% malathion active ingredient and is a repackage of the technical material therefore it has a low acute oral, dermal, and inhalation toxicity (Toxicity Category III or IV). The safety data sheet (FMC, 2017b) reported an acute oral LD_{50} of approximately 5,500 mg/kg to rats (IV), an acute dermal LD_{50} of >2,000 mg/kg to rabbits (III), and an acute inhalation LC_{50} of >5.2 mg/L (IV) in a 4-hour exposure to rats.

2.4.5 Subchronic and Chronic Toxicity

A 21-day dermal toxicity study in rabbits (94% a.i.) reported a benchmark dose level ($BMDL_{20}$[1]) of 135/143 mg/kg/day (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/day (females) and BMD_{10} of 124 mg/kg/day 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. Based on 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

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

[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.

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 NOAEL values of 1,000 mg/kg and 4 mg/kg/day, respectively. The acute and subchronic LOAELs were 2,000 mg/kg based on decreased motor activity, such as tremors, and plasma and red blood cell AChE inhibition; 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).

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 the 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 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

USEPA classifies malathion as "suggestive evidence of carcinogenicity but not sufficient to assess human carcinogenic potential" by all exposure routes (USEPA, 2016b). Animal cancer bioassays in mice and rats on malathion show "suggestive evidence of carcinogenicity" but these data are insufficient to assess the carcinogenic potential of malathion. There is a relatively large epidemiology database concerning malathion due to the high prevalence of malathion as an insecticide and long duration of malathion use in agriculture and the residential environment. USEPA's evaluation of a variety of health outcomes from the majority of these studies indicate that the available published data shows no evidence of a specific association with malathion use although there were some suggestive associations in which malathion may play a role in the health outcome (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.

The International Agency for Research on Cancer (IARC) concluded malathion is probably carcinogenic to humans (Group 2A) based on sufficient evidence in experimental animals and limited evidence for cancer in humans, but with positive associations observed for non-Hodgkin lymphoma and cancer of the prostate (IARC, 2016). The IARC report is the only report that suggests malathion is a carcinogen. Evaluations by pesticide regulatory agencies in the United States and other countries where malathion is registered have concluded that malathion is not a carcinogen.

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 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

A 2011 USEPA acceptable guideline immunotoxicity study in mice (MRID 48550501) reported a NOAEL of 1,215.8 mg/kg/day (7,000 parts per million (ppm), highest dose tested) without the establishment of a LOAEL for immunotoxicity. The study 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). Other studies that haven't been conducted as a guideline study to support malathion registration suggest that malathion may affect the immune system (ATSDR, 2003; US FS, 2008), however these effects occur at doses not anticipated from Program use.

2.4.11 Toxicity of Other Ingredients

Fyfanon® ULV AG contains 3.5% other ingredients. Specific compounds are not listed for these ingredients and are considered confidential business information. Available acute toxicity data from the safety data sheet of Fyfanon® ULV AG (FMC, 2017b) suggests similar toxicity to the technical active ingredient. Storage of Fyfanon® ULV AG at high temperatures may form a more toxic and synergistic contaminant, isomalathion (acute oral LD_{50} of 89 mg/kg in rats). Inhalation of isomalathion or malathion can cause organophosphorous poisoning with symptoms such as headache, nausea, vomiting, blurred vision, tightness in chest, drooling, frothing of mouth and nose, convulsions, coma, and death.

2.4.12 Fire Hazards

The safety data sheet (FMC, 2017b, Cheminova, Inc., 2010) indicates that Fyfanon® ULV AG is non-flammable. However, burning of malathion generates noxious and toxic fumes, and hazardous combustion products (carbon oxides, oxides of phosphorus, oxides of sulphur, dimethyl sulfide, methyl mercaptan, irritating fumes and smoke). The largest health threat from smoke is from fine particles that are a common component of fire. These microscopic particles can penetrate deep into the lungs and can cause a range of health problems, from burning eyes and a runny nose to aggravated chronic heart and lung disease.

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 22 times more toxic than malathion.

Malathion is classified as "suggestive evidence of carcinogenicity, but not sufficient to assess human carcinogenic potential". USEPA uses a non-linear approach (i.e., the chronic reference dose) for all chronic toxicity data 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, 2016e). 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 area (USEPA, 2016b).

3.2 Ecological Dose-Response Assessment

The below provides a summary of malathion effects toxicity data for non-target fish and wildlife. A large amount of data has been collected for malathion and the below is not meant to summarize all toxicity data but to capture the range of sensitivities using peer review literature and data submitted to USEPA to support registration of pesticide data. Much of the effects data has recently been summarized by USEPA with additional analysis being conducted by the registrant for malathion (USEPA, 2016g; FMC, 2019). These documents provide the reader with a more in-depth analysis of the non-target toxicity data for malathion and its associated metabolites.

3.2.1 Wild Mammal, Avian and Reptile Toxicity

The acute toxicity of malathion to mammals is summarized above in section 2.4, Hazard Identification. In general, malathion has moderate acute oral toxicity and low inhalation and dermal toxicity to mammals based on available data.

The acute oral median lethal doses for birds range from 150 mg/kg to chickens to 1,485 mg/kg to 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
Sharped-tailed grouse, *Tympanuchus phasianellus*	LD_{50}	220 mg/kg	USEPA, 2006b
Ring-necked pheasant, *Phasianus colchicus*	LD_{50}	136 mg/kg	USEPA, 2016f
Horned lark, *Eremophila alpestris*	LD_{50}	403 mg/kg	USEPA, 2006b
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, 2006b
Northern bobwhite quail, *Colinus virginianus*	LC_{50}	3,497 ppm	USEPA, 2006b
Japanese quail, *Coturnix japonica*	LC_{50}	2,962 ppm	USEPA, 2006b
Mallard duck, *Anas platyrynchos*	LC_{50}	>5,000 ppm	USEPA, 2006b

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, *Sturnis 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, *P. 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.

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 (McLean et al., 1975; Baker, 1985). 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 for *P. cinereus* at any test concentration (Baker, 1985).

Laboratory toxicity testing using reptiles is less extensive than data available for amphibians. Holem et al. (2006) noted 20% mortality in the western fence lizard (*Sceloporus occidentalis*) after oral dosing of 200 mg/kg of Fyfanon® ULV, the insecticide product of malathion used in the program. 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. 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. 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 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 contact LD_{50} values in honeybees range 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, 2012a). 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 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 reported 24-hour 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 (2006b) reported seven 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; Ilnytzky and Marshall, 1974; Chakraborti et al., 1983). A variety of agronomically important crops has 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* (Mayer and Ellersieck, 1986; Beyers et al., 1994; US FS, 2008) (figure 3-1; appendix A-1). USEPA (2016g) reports a similar range of sensitivities to fish with values ranging from 4.0 to 448,000 µg/L. FMC (2019) in an evaluation of available malathion fish toxicity data proposes that the proposed endpoint for evaluating acute risks to fish is the LC_{50} value of 52 µg/L reported for bluegill sunfish. Criteria for acceptability of previously conducted studies were used to select those studies conducted under standardized test protocols for evaluating fish toxicity to pesticides.

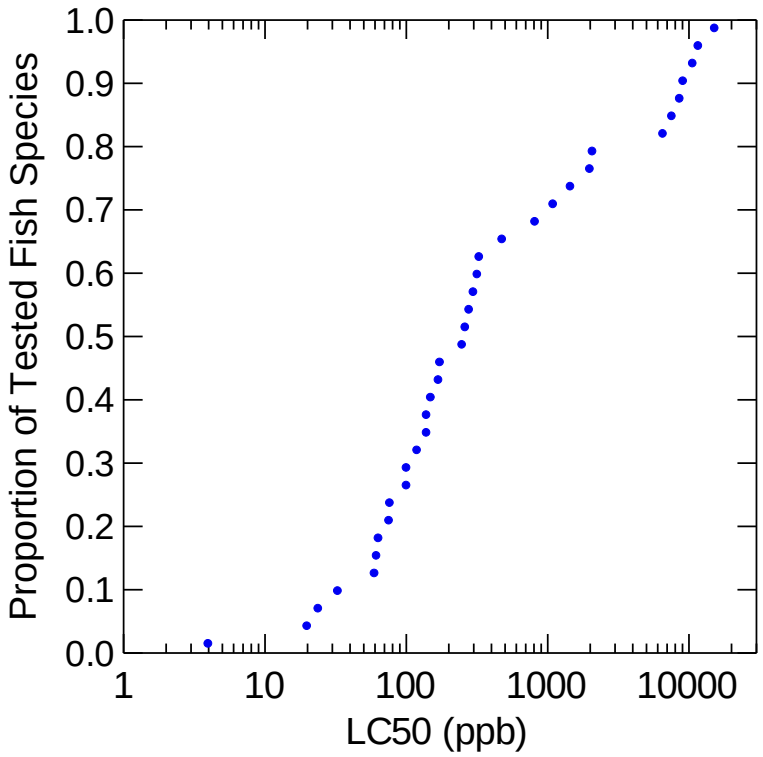

Figure 3-1. Acute toxicity of malathion to freshwater and saltwater fish species

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 test 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, 2006b). 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, 2006b). 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 allowable/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, 2006b).

Acute toxicity to amphibians is variable based on the sensitivity of different species and time of exposure. FMC (2019) in a review of amphibian toxicity data reports an African-clawed frog LC_{50} value of 4.7 mg/L. Relyea (2004) tested the survival rates of six species of tadpoles over a sixteen 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} values 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% emulsifiable 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 of 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.

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 (Tchounwou et al., 1991; Keller and Ruessler, 1997) (figure 3-2, appendix A-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). USEPA (2016g) reports a wider range of sensitivities for aquatic invertebrates reporting a more sensitive value for the freshwater cladoceran, however a majority of the reported toxicity values in the USEPA analysis are captured in the below distribution of sensitivities. The reported lower cladoceran median lethality value is a lowest observable effect concentration and not directly comparable to median lethality or effect concentrations. FMC (2019) in a review of aquatic toxicity data to provide proposed effects metrics for non-target species proposes using the D. magna EC_{50} value of 0.70 µg/L which falls within the distribution of acute lethality values presented in figure 3-2.

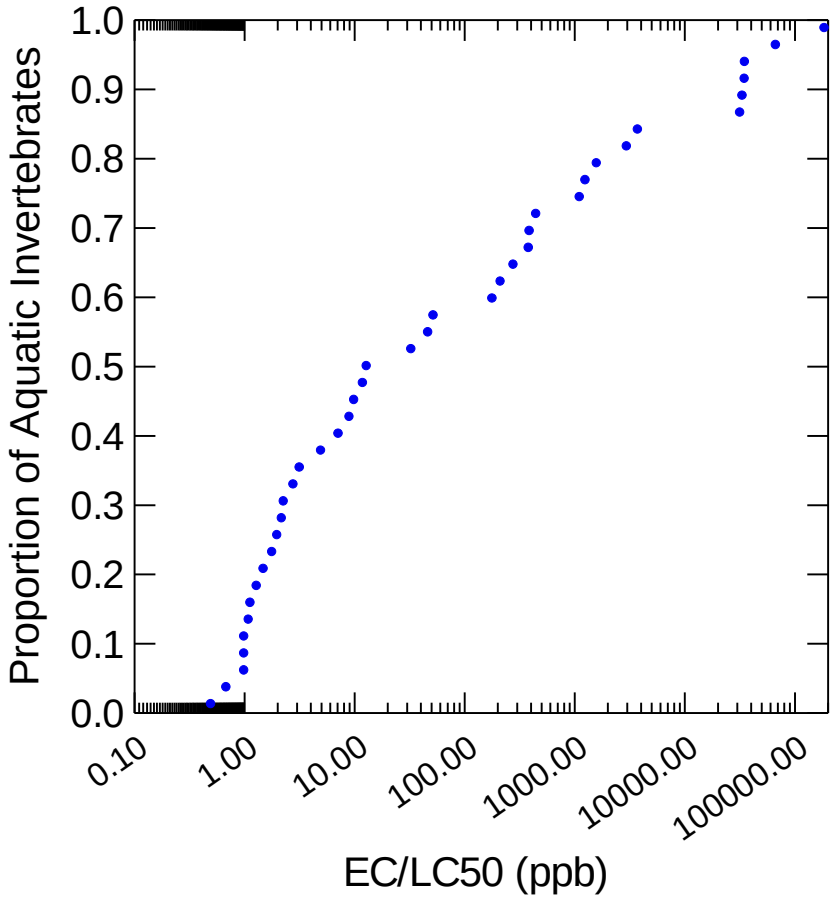

Figure 3-2. Acute aquatic invertebrate toxicity distribution for malathion.

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 *D. 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, are 320 and 0.26 µg/L, based on 9-day and 24-hour exposures. Relyea (2005) reported NOEC values of 320 µg/L, for 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, 2006b).

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 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 parts per billion (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 three 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 program applications of malathion.

3.2.7 Formulation and Metabolite Aquatic Toxicity

Fyfanon® ULV, is composed of 96.5% malathion and contains a relatively minor quantity of other ingredients. Fyfanon® ULV is a repack of the technical material and therefore the toxicity studies conducted using the technical material are representative of the proposed end-use product used by the Program.

Several metabolites of malathion can occur in aquatic environments however they occur only in trace levels and are not considered to be of toxicological concern. USEPA (2006b) 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 (median tolerance limit or TLm) for each of the metabolites (table 3-2).

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.

Table 3-2. 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

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 3-3). FMC (2019) reports that malaoxon is 0.80 to 2.58 times more toxic to fish than malathion based on data that were determined to meet their criteria for acceptability. The conversion of malathion to malaoxon in aquatic environments can range from approximately 1.8 to 10% (CDPR, 1993; Bavcon et al., 2005; USEPA, 2012a). 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, 2012a). 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 3–3. 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, 2012a
Killifish, *Oryzias latipes*	48-hour LC_{50}	280	1,800	Tsuda et al., 1997
Bluegill sunfish, *Lepomis macrochirus*	96-hour LC_{50}	52	62.6	FMC, 2019
Rainbow trout, *Onchorynchus mykiss*	96-hour LC_{50}	174	67.4	FMC, 2019
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, 2012a
Cladoceran, *Daphnia magna*	48-hour EC_{50}	0.294	0.70	FMC, 2019

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, the potentially exposed human populations and complete exposure pathways are identified, and then exposure for the identified human populations are qualitatively or quantitatively evaluated in this section.

4.1.1 Identification of Potentially Exposed Human Populations and Complete Exposure Pathways

Workers in the program are the most likely human population segment to be exposed to malathion during grasshopper treatments. 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 ULV spray will be minimal with adherence to label requirements, the use of personal protective equipment (PPE), general safety hygiene practices, and restricted entry intervals into treated areas after application (Cheminova, Inc., 2012). The label-required PPE includes long-sleeved shirt and long pants, shoes plus socks, and chemical-resistant gloves made of barrier laminate or butyl rubber, nitrile rubber, or viton. The safety datasheet also recommends safety glasses with side-shields or chemical splash goggles for eye protection, and suitable respiratory equipment in case of inadequate ventilation or risk of inhalation of mists or vapors (Cheminova, Inc., 2010). The occupational exposure limits (8 hour time weighted average) for malathion are 15 mg/m^3 (total dust) (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 ULV spray applications may occur, but will be reduced by adherence to the label requirement of using the largest droplet size consistent with acceptable efficacy and minimizing formation of very small droplets by selecting appropriate nozzle size, orienting nozzles away from the air stream and avoiding excessive spray boom pressure (Cheminova, Inc., 2012). Accidental exposure to malathion may occur for a worker during application. This accidental exposure scenario is further quantified in the next section (4.1.2).

Malathion exposure to the general public is not expected from the program use based on label requirements and program standard operating procedures (USDA APHIS, 2016a) that prevent potential exposure. Only protected handlers may be in the area during application, and entry of the general public into the treated area is not allowed during the re-entry interval period. APHIS treatments are conducted on rural rangelands, where agriculture is a primary economic factor and widely scattered dwellings in low population density ranching communities are found. The program aerial application statement of work (2016a) requires avoiding flights over congested areas, water bodies, and other sensitive areas. Aerial applications are not allowed while school buses are operating in the treatment area; within 500 feet of schools or recreational facilities; when wind velocity exceeds 10 miles per hour (mph) (unless a lower wind speed is required under State law); when air turbulence could seriously affect the normal spray pattern; and/or temperature inversions could lead to off-site movement of spray. The program also notifies

residents within treatment areas, or their designated representatives, prior to application to reduce the potential for incidental exposure (USDA APHIS, 2014).

The primary use for areas where the program may apply malathion includes rangeland that could be grazed by livestock. Farmers in areas near proposed suppression areas may grow crops such as alfalfa and corn that are used for livestock. They also grow potatoes, sugar beets, wheat, barley, sweet corn, beans, and a variety of other crops (USDA APHIS, 2016b). Exposure to the general public from malathion through dietary food consumption (meat and dairy products) at levels higher than established tolerance levels for malathion is not expected based on the proposed use pattern for the program which includes reduced application rates compared to those on the label.

Malathion has environmental fate properties that suggest a potential for transport to surface and groundwater (Section 2.3). However, the potential exposure of the general public to malathion from drinking water sources from program use is not expected based on adherence to the label requirements, the proposed use rates, and APHIS program treatment guidelines (such as the use of 200- and 500-foot ground and aerial application buffers, respectively) (USDA APHIS, 2016a; 2017).

4.1.2 Exposure Evaluation

This section quantitatively evaluates potential accidental worker exposure from dermal contact and inhalation exposure routes while mixing and loading based on the program application rates and a label required closed system (i.e., a sealed pesticide transfer device). The quantified potential accidental worker exposures are acute or short-term. Long-term exposure to malathion for workers is not expected because only one application is proposed per season. The typical application rates for malathion treatments in the program are 0.62 lb a.i./acre (conventional) and 0.31 lb a.i./acre (RAATs) with approximate total applied volumes of 8 fl oz/acre (conventional) and 4 fl oz/acre (RAATs).

To quantify the potential accidental exposure to workers during mixing and loading via dermal and inhalation pathways, APHIS estimated dermal and inhalation doses using the following equation:

> Dermal Dose = Application Rate (lb a.i./acre) × Area Treated (acre/day) x Dermal Unit Exposure (µg/lb a.i.) × Conversion Factor (0.001 mg/µg)) ÷ Body Weight (BW) (kg)
>
> Inhalation Dose = (Application Rate (lb a.i./acre) × Area Treated (acre/day) x Inhalation Unit Exposure (µg/lb a.i.) × Conversion Factor (0.001 mg/µg)) ÷ BW (kg)

The mixing/loading liquids exposure scenario in the Occupational Pesticide Handler Unit Exposure Surrogate Reference Table is the closest to the program loading and application exposure scenario (USEPA, 2016b).

The dermal unit exposure of 37.6 µg/lb a.i. (single layer, gloves PPE level), and inhalation unit exposure of 0.219 µg/lb a.i. (no respirator PPE level) of the mixing/loading liquids exposure scenario was used for the exposure estimates. Dermal and inhalation doses were quantified for

maximum and average exposure scenarios based on conventional and RAATs application rates of 0.62 and 0.31 lb a.i. per acre. Area treated was assumed 100 acres per day. A body weight of 69 kg for a woman was used as a conservative estimate of exposure. The exposure dose estimates for dermal and inhalation routes are included in appendix B.

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 a.i., soil or foliar dissipation half-life, application interval, and number of applications to calculate exposure concentrations on a variety of food items. For foliar sprays the estimates of exposure are based on the original Kenaga nomogram using 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

The method of calculating aquatic exposure concentrations for the program was through the use of two aerial drift deposition models. The models (AgDrift and AgDisp) allow for specific application information to be used as input into the model, and then determine the amount of drift that would occur at a user-defined distance from the spray block. The difference between deposition at the edge of a field and a selected buffer zone can be used as a means to reduce the total amount of insecticide that would be expected at a certain distance from the spray block. Buffer zones, in addition to the previously mentioned mitigation measures, can be established based on the reduction in exposure to levels that would not be expected to result in direct or indirect effects to individuals, populations, or species as a whole.

AgDrift and AgDisp are pesticide drift deposition models that provide the user with the ability to provide site- and application-specific information as input to determine application efficiency and off-site drift residues. AgDisp is a model which was developed by the U.S. Department of Agriculture 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).

For this risk assessment, the AgDrift model was used to simulate all ground applications, while AgDisp was used to simulate all aerial ULV applications. The AgDisp model was used in the aerial applications to assess buffer distances and application heights that are beyond those that have been validated using AgDrift (Teske and Thistle, 2004). Input data for the AgDrift and AgDisp models were based on the product label and specific application information available in the APHIS work plan for the program (USDA APHIS, 2016a). While several types of aircraft are available for application in the program, the quantitative differences in drift are minimal at the buffer zones being assessed. Therefore, the focus of the modeling work was to emphasize those parameters that have the greatest influence on drift. Multiple factors can influence pesticide drift; however, release height, wind speed and direction, and nozzle atomization/orientation are the primary factors influencing drift (Bird et al., 1996; Teske et al., 2000).

Unless otherwise specified, release height for aerial applications was set at 75 feet with a maximum allowed sustained wind speed of 10 mph, and the American Society of Agricultural and Biological Engineers (ASABE) droplet size distribution of fine to very fine (median diameter = 137.5 µm). ASABE has developed standardized parameters for different droplet size spectra that can be selected in both drift models. The very fine-to-fine droplet size spectrum selected for all of the air and ground ULV simulations is consistent with an application recommended for use in the program. Application rates selected for modeling were based on the maximum RAATs rates assuming 100% coverage during application. Lower RAATs rates may be used in cases where reduced application and coverage can be implemented to effectively suppress grasshopper and Mormon cricket populations.

The intent of the program is to make applications as close to the ground as possible. However, in some cases where rapid elevation changes are likely to occur, applications must be made at a height that will ensure pilot safety and the appropriate swath width. All applications were simulated on an area where the buffer was on a zero grade and there was no upslope or downslope between the spray block and sensitive habitat. In addition, the maximum height of vegetation between the spray block and habitat was no greater than 0.1 meters high. This provides a conservative estimate regarding the ability of plants and terrain to intercept drift between the spray block and sensitive areas.

A sustained 10 mph wind speed was used as a representative maximum that is allowed in program applications in all simulations. The wind direction was assumed to be at -90^{o} directly

towards the sensitive habitat for the entire length of all swaths with no reduced area of application occurring over the spray block.

Other parameters that influence drift are meteorological conditions. In addition to wind speed, both drift models allow the user to input temperature and humidity. Temperature and humidity values for this exercise were selected from all geographically representative areas where the program could potentially make applications. Meteorological data was obtained from the AgDisp model which allows the user to view a 30-year compendium of meteorological data from 239 sites in the United States (1961–1990 National Solar Radiation Data Base, Version 1.0, Solar and Meterological Surface Observational Network) (Teske and Curbishley, 2003).

The 25th percentile humidity value and the 75th percentile highest temperature were selected based on weather data from Lubbock, Texas, which reported a temperature value of (90 ^{o}F) with a humidity value of 36%. Bismarck, North Dakota, and Pocatello, Idaho, were also evaluated, and based on a combination of maximum temperature and minimum humidity values for those areas, all three had similar application efficiencies and drift fractions based on their respective worst-case temperature and humidity values. Therefore, the temperature and humidity value from Lubbock, Texas, was used because it would maximize the potential for insecticide drift.

AgDisp and AgDrift provide estimates of off-site residues related to drift in terrestrial and aquatic environments. However, they do not provide an estimate of the amount of runoff that could occur into aquatic habitats. Several aquatic fate models exist to estimate environmental loading into aquatic habitats. USEPA/OPP has developed a tiered approach for the use of aquatic fate models that allow the user to estimate aquatic concentrations based on default "reasonable worst-case conditions," or to calculate estimated aquatic concentrations based on crop-specific soil and weather conditions (USEPA, 2004). None of the available models allow the user to calculate the effects of application buffers in reducing pesticide runoff.

The runoff contribution from applications in the program is considered minimal due to the application buffers that are applied adjacent to aquatic environments. The effectiveness in the use of application buffers to reduce runoff can vary based on site conditions, the type of vegetation present in the buffer, and the fate of the insecticide. However, the products used in the program, the large buffers, and other label specifications and APHIS policies, ensure that runoff will not be a significant contribution of off-site pesticide movement.

Aquatic residue estimates were made using the program's 200-foot ground and 500-foot aerial no treatment buffers. Water body size were one acre in area and 6.56 feet deep to simulate a pond scenario, and one acre in area and 0.49 feet deep to simulate a wetland scenario. All residues were average acute values assuming a static system with no degradation of the insecticide over time. Acute 96-hour residues from ground applications ranged from 83.21 to 1,110 parts per trillion (ppt) while acute 96-hour aerial application residues ranged from 5.87 to 7.62 ppb. Chronic 21-day residues from ground applications ranged from 1.63 to 22 ppt while acute 21-day aerial application residues ranged from 0.046 to 0.15 ppb. The 96-hour and 21-day residues were estimated using a first order rate half-life equation and an aquatic half-life of 3 days. These are considered conservative estimates based on assumptions in the model and when compared to monitoring data that has been collected to validate field applications (USDA APHIS, 2015b).

5.0 RISK CHARACTERIZATION

Risks associated with potential adverse effects are characterized qualitatively and quantitatively in this section. Results from the risk characterization suggest that the use of malathion ULV spray for the grasshopper and Mormon cricket suppression 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 cholinesterase through oral, inhalation and dermal exposure. The low potential for significant exposure from the program ULV application of malathion suggests there are minimal risks to workers.

Accidental exposure during mixing and loading in a closed system for the ULV-application may occur even though it is an unlikely event. APHIS quantified the risks from potential dermal and inhalation exposure for workers and calculated a hazard quotient (HQ) using the following equation for non-carcinogens:

HQ = Exposure Dose / Reference Dose

Only non-cancer risk was evaluated because USEPA classified malathion as "suggestive evidence of carcinogenicity but not sufficient to assess human carcinogenic potential". Table 5-1 summarizes the results for accidental direct contact exposures. The acute oral reference dose of 0.1 mg/kg/d is the appropriate toxicity value because an accidental exposure is considered an infrequent occurrence and dermal or inhalation RfDs are not available. The calculated dermal HQs of 0.3/0.2, inhalation HQs of 0.002/0.001, and combined dermal and inhalation HQ values of 0.3/0.2 under the maximum (conventional application rate) and average (RAATs application rate) exposure scenarios (table 5-1) are all below the USEPA's level of concern (HQ=1), indicating no concerns for adverse health risk. The risk calculations are included in appendix B.

Table 5-1. Hazard quotients estimated for dermal and inhalation exposures of workers.

	Dermal Exposure Maximum/Average	Inhalation Exposure Maximum/Average
Exposure intake or dose (mg/kg-day)	3.4E-02/1.7E-02	2E-04/9.8E-05
Reference dose (mg/kg-day)	0.1	0.1
HQ	**0.3/0.2**	**0.002/0.001**
Combined dermal and inhalation HQ = **0.3/0.2**		

The risks to the general public in the treatment areas from ground or aerial applications are not expected because APHIS treatments are conducted in rural rangeland areas where agriculture is a

primary economic factor, and widely scattered dwellings in low population density ranching communities are found. Historically, a majority of the applications have occurred on Federal lands. The program notifies residents and implements mitigation measures beyond label requirements to ensure that no treatments occur within the required buffer zones from structures, such as homes and schools where there is potential exposure for residents including children (USDA APHIS, 2016a). There are no adverse health risks associated with eating treated food because the program treatments occur in rangeland and there is no primary food consumption pathway from direct intake of crops. Adverse health risks from indirect consumption of cattle grazed on the treated rangeland are not expected because of the low application rate of the ULV treatment and natural degradation of the malathion.

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 chronic NOEL (3 mg/kg/day) from a cholinesterase inhibition study where daily dosing of malathion occurred for two years. 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 bw/day)	Ingestion (wet) (g/day)	% body weight consumed	(kg-diet/day)	Adjusted Acute NOEL	Adjusted Chronic NOEL
Herbivores/	15	3	14	95	1.43E-02	2,197.83	6.59
Insectivores	35	5	23	66	2.31E-02	1,778.28	5.33
	1000	31	153	15	1.53E-01	769.16	2.31
	15	3	3	21	3.18E-03	2,197.83	6.59
Granivores	35	5	5	15	5.13E-03	1,778.28	5.33
	1000	31	34	3	3.40E-02	769.16	2.31

Using the residues expected from a full application of malathion and comparing those concentrations to the adjusted toxicity endpoints, all acute risk quotient values were well below 1 with the highest value reported for 15 and 35 g mammals that feed exclusively on contaminated short grass (table 5-3). However, chronic risk quotient values ranged from 0.07 to 10.76 suggesting chronic risk for certain mammal groups that feed within treated areas.

Table 5-3. Calculated mammalian risk quotient values for malathion assuming no application buffer zone.

Dose-based RQs (Dose-based EEC/ NOEL)	15 g mammal		35 g mammal		1000 g mammal	
	Acute	Chronic	Acute	Chronic	Acute	Chronic
Short Grass	0.03	10.76	0.03	9.19	0.01	4.93
Tall Grass	0.01	4.93	0.01	4.21	0.01	2.26
Broadleaf plants/small insects	0.02	6.05	0.02	5.17	0.01	2.77
Fruits/pods/large insects	0.00*	0.67	0.00	0.57	0.00	0.31
Seeds (granivore)	0.00	0.15	0.00	0.13	0.00	0.07

*Values are less than 0.001

The effects data point for estimating chronic risk 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 for a 2-year period. This type of situation would not occur with program malathion applications because it can only be applied once per year and residues would not persist due to the rapid breakdown of the parent and other toxic metabolites, such as malaoxon.

Direct acute and chronic risk of malathion to mammals is expected to be minimal from all malathion application methods, but there is the potential for indirect effects from habitat alteration and loss of food items. 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 and a complete loss of invertebrates from a treated area is not expected because of low program rates and application techniques. In addition, aerial and ground application buffers and untreated swaths using RAATS provide refuge for invertebrates that serve as prey for insectivorous mammals and would encourage repopulation of areas that may have been treated.

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 (1978) 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 greater than three 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 (136 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 69.54 to 125.05 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 weight consumed	(kg-diet/day)	Adjusted LD_{50} (mg/kg-bw)
Small	20	5	23	114	2.28E-02	69.54
Mid	100	13	65	65	6.49E-02	88.53
Large	1000	58	291	29	2.91E-01	125.05

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 1.22 (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 (Dose-based EEC/adjusted LD_{50})	Avian Acute RQs 20 g	100 g	1000 g
Short Grass	1.22	0.55	0.17
Tall Grass	0.56	0.25	0.08
Broadleaf plants/small insects	0.69	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 with the exception of the chronic quotient value calculated for birds that would feed exclusively on short grass (table 5-6). These risk quotient values are based on the maximum application rate for malathion with no application buffer zone and upper bound estimates of residues for birds.

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

Dietary-based RQs	**RQs**	
(Dietary-based EEC/LC_{50} or NOEC)	**Acute**	**Chronic**
Short Grass	0.05	1.31
Tall Grass	0.02	0.60
Broadleaf plants/small insects	0.03	0.73
Fruits/pods/seeds/large insects	0.00*	0.08

*Values are less than 0.001

Based on the assessment above, direct avian acute and chronic effects are expected to be minimal. The assessment is conservative because the residues are based on upper bound estimates and assume that all affected birds will feed exclusively on one type of food item, and that all of the food they consume will have maximum malathion residues. With the use of RAATs it is unlikely that birds will only feed on contaminated food items during the duration that residues are present. In addition, malathion degrades quickly in the environment and residues on food items are not expected to persist, therefore chronic risks are not anticipated. Chronic risks were based on toxicity endpoints assuming multiple weeks of daily exposure to birds which would not occur in field applications.

Possible indirect risks to birds are expected to be minimal based on the discussion of indirect risks to mammals from malathion applications. Indirect effects to habitat and food items are not expected because of malathion's low toxicity to plants and the implementation of application buffer zones and the use of RAATs that will reduce the potential impacts to invertebrates that serve as prey for avian species.

The possible indirect effects of malathion applications to birds have been evaluated in several field studies. 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./acre), 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. Pre-spray grasshopper densities were relatively low (1 to 4 per square yard) on all plots and were significantly reduced in the post-spray period. This probably made the food availability test even more rigorous than would be posed by an actual operational grasshopper suppression project, where pre-spray densities are much higher and even post-spray grasshopper densities usually exceed 1 or 2 per square yard (McEwen et al., 1996).

George et al. (1995) evaluated the effects of grasshopper malathion applications on vesper parrow (*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 RAATs 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 show a range of amphibian toxicity values for several species of frog tadpoles from 0.56 to 13.27 mg/L. Expected aquatic residues from malathion applications range from 0.083 to 7.62 µg/L when program restrictions for applications adjacent to aquatic habitats are implemented. Residues are approximately 73 times below the most sensitive acute toxicity value for malathion, suggesting low acute direct effects from malathion applications. 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 65 times above the highest concentration that was estimated in this assessment suggesting, a low probability of sublethal risk from malathion exposure to amphibians when implementing program measures near aquatic habitats. Indirect risk is also expected to be low based on results of the aquatic risk characterization. Program protection measures and the available toxicity data for fish, aquatic invertebrates, and plants suggest that no indirect effects related to reductions in habitat or aquatic prey items would be anticipated from malathion applications. Adult amphibians that may forage for terrestrial invertebrates away from aquatic breeding sites could also be at risk from the loss of prey items. However, the implementation of application buffers and other program restrictions from breeding sites, and the available field data regarding malathion impacts to non-target terrestrial invertebrate populations, would suggest that indirect effects would not be expected to occur (Smith et al., 2006).

For reptiles, available data regarding malathion reptile toxicity suggest that no lethal or sublethal impacts would be anticipated because of program measures to protect them. However, the effects data for reptiles is limited; thus, the avian risk assessment will be used to determine the potential for risk. Program measures for the protection of birds from direct effects of malathion applications would also be protective for reptiles. Indirect risk to reptiles from the loss of food items is expected to be low since impacts to food items such as plants is low and not all terrestrial invertebrates will be affected due to the low application rates and use of RAATs.

5.2.1.4. Risk to Terrestrial Invertebrates

Risks to terrestrial invertebrate populations are anticipated based on the available toxicity data for invertebrates and the broad-spectrum activity of malathion. Full treatments (i.e., maximum application with no RAATs) of malathion to control grasshopper populations have been shown to have negative impacts to non-target terrestrial invertebrates, including some coleopterans and field crickets, within the first week of application (Swain, 1986; Quinn et al., 1990). The risk to terrestrial invertebrates can be reduced by the implementation of application buffers and the use of RAATs, which will reduce exposure and create refuge areas where malathion impacts will be reduced. Smith et al. (2006) conducted field studies to evaluate the impacts of grasshopper treatments to non-target terrestrial invertebrates and found minimal impacts when making reduced applications with a reduced coverage area for a ULV formulation of malathion. The potential for long-term exposure and effects to terrestrial invertebrates decreases quickly because the residual toxicity of malathion is approximately 4 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 terrestrial plants. There is the potential for indirect effects to 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 demonstrate 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 more than five times the proposed RAATs rate (USEPA, 2012b). However, risk to pollinators is reduced because of the short residual toxicity of malathion and the use of application buffer zones from sensitive plant species. In addition, the incorporation of other mitigation measures such as the use of RAATs and wind speed/direction mitigations that are designed to minimize exposure, reduces the potential for impacts to terrestrial invertebrates.

5.2.2 Aquatic Risk Characterization

Available acute and chronic effects data for malathion and fish were above the 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 fish from malathion are not expected. Consumption of contaminated prey is not expected to be a significant pathway of exposure for aquatic species based on expected residues and the low BCF.

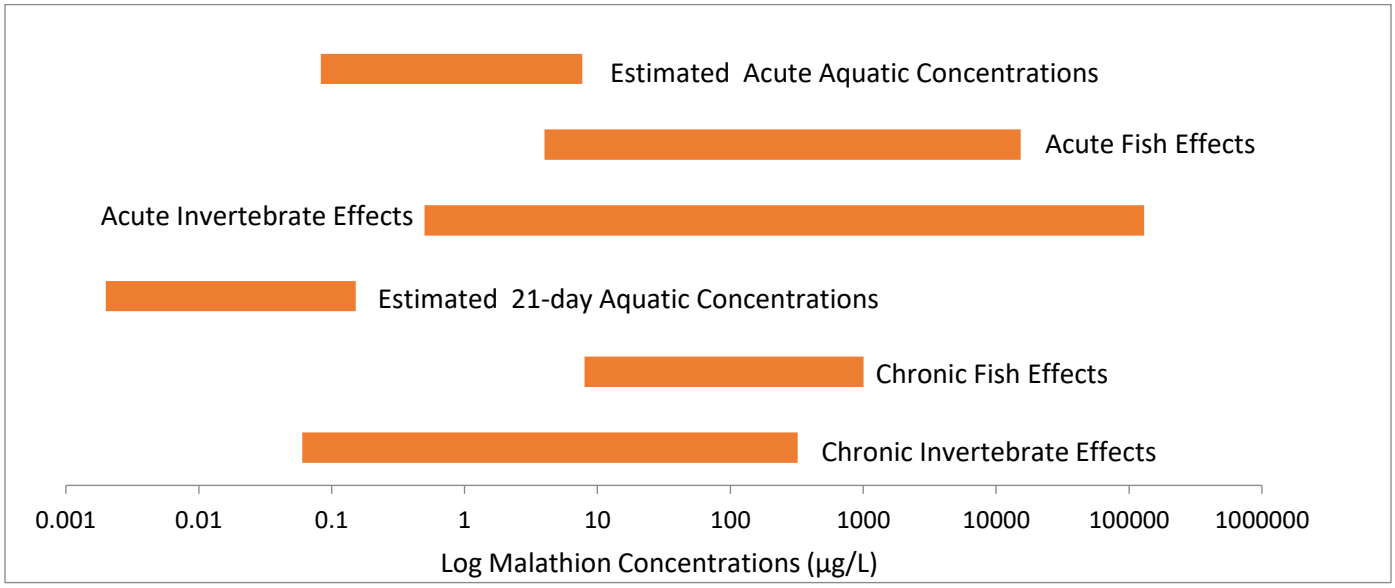

Figure 5-1. Malathion risk characterization for fish and aquatic invertebrates.

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 approximately two orders of magnitude, or greater, below the NOEC.

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 that estimated residues are not expected to result in impacts to aquatic prey items for aquatic species. The estimated residues from aerial applications suggest acute and chronic risk to some aquatic invertebrates. However, as previously mentioned, these residues are considered conservative estimates when compared to observed residues that have been measured in the field. Average residue values collected from drift cards collected at 500 feet from actual applications were greater than 20 times lower than values determined using the drift models. In addition, the lowest chronic effect endpoint is based on a 21-day continuous exposure which would not occur in this program because only one application is made per season and malathion degrades rapidly in aquatic environments.

USEPA (2006b) 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 10 µg/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 human health and ecological risk assessments with any environmental stressor. In addition, there is uncertainty in where treatments may occur in the United States, and the extent of malathion use in a given infestation because its use is based on site-specific factors. APHIS may conduct a treatment to suppress economically damaging grasshopper and/or Mormon cricket populations on rangeland in 17 Western States (Arizona, California, Colorado, Idaho, Kansas, Montana, Nebraska, Nevada, New Mexico, North Dakota, Oklahoma, Oregon, South Dakota, Texas, Utah, Washington, and Wyoming). However, rangeland does not occur over the entire area of most of those States. Should grasshopper or Mormon cricket populations reach economically damaging levels, APHIS could conduct a treatment on rangeland in any of the 17 Western States (USDA APHIS, 2015b).

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 registered commercial agriculture, industrial, and household uses in addition to governmental uses. However, the total agricultural acres treated with malathion has decreased by 75%, and annual pounds applied has decreased 61% since its peak in 1998 (USEPA, 2018). Use data for malathion shows that the recent annual average use of malathion in the US is approximately 1 million pounds for agricultural uses and approximately 1.7 million pounds for non-agricultural uses (USEPA, 2018). Between 2011 and 2015, there was an annual average of approximately 856,000 pounds of malathion applied to an average of 685,000 acres for agricultural use. In comparison, the APHIS grasshopper program use of malathion in rangelands is much less compared to normal agricultural use. During the past decade, only one malathion treatment was applied to a total of 1,744 acres in South Dakota in 2009. The most common applications for the program are carbaryl bait or diflubenzuron treatments and greater than 99% of the total number of applications between 2006 and 2017 used RAATs. The size of treatment blocks varies with areas as small as 30 acres to greater than 219,000 acres. Grasshopper treatment areas greater than 3,000 acres have been treated almost exclusively with diflubenzuron, with the exception of carbaryl bait applications for Mormon cricket control in Utah (USDA APHIS, 2015b). The program will apply only one of the insecticides that are available and only one application in any given season. The use of malathion is unlikely to be in conjunction with other insecticide uses; however, there may be herbicide use on rangeland but the level of treatment will depend on the value of the rangeland and whether treatments are warranted.

Cumulative impacts from the potential for co-exposure of malathion and other chemicals used in the program that have a similar mode of action resulting in synergism, potentiation, additive, or antagonistic effects are not expected. Malathion inhibits the enzyme AChE in the central and or peripheral nervous system. Although organophosphorus pesticides have the same mode of action, their potency for cholinesterase inhibition varies. Malathion is a less potent inhibitor of red blood cell cholinesterase and the least potent inhibitor of brain cholinesterase (USEPA, 2002; 2006a). The other insecticides used within the grasshopper program include diflubenzuron, carbaryl, and

chlorantraniliprole. Diflubenzuron and chlorantraniliprole do not have the same mode of action as malathion. Diflubenzuron is an insect growth inhibitor and affects the hematopoietic system in mammals. Chlorantraniliprole acts on the ryanodine receptor. Although carbaryl also targets the nervous system (carbamylation of AChE resulting in accumulation of the neurotransmitter, acetylcholine), it will not be applied at the same time as malathion because the program only uses one of the insecticides and makes only one application in a given area per growing season. Insecticides may be used in watersheds where rangeland and agricultural lands occur. This could include organophosphate insecticides such as malathion as well as other pesticides. The use and occurrence of these insecticides will vary temporally and spatially so it is difficult to state whether program treatments could result in off-site residues with other pesticides. Label restrictions and program requirements are designed to minimize exposure to the public and non-target wildlife, reducing the potential for mixtures of pesticides, or other chemicals, to occur with program treatments.

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Appendix A-1. Malathion acute fish toxicity values

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

Appendix A-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, 2006b
Simocephalus serrulatus	96-hour LC_{50}	0.69 µg/L	USEPA, 2006b
Isoperla sp.	96-hour LC_{50}	0.69 µg/L	USEPA, 2006b
Daphnia magna	96-hour LC_{50}	1.0 µg/L	USEPA, 2006b
Pteronarcella badia	96-hour LC_{50}	1.1 µg/L	USEPA, 2006b
Limnephalus sp.	96-hour LC_{50}	1.3 µg/L	USEPA, 2006b
Gammarus lacustris	48-hour EC_{50}	1.8 µg/L	USEPA, 2006b
Daphnia pulex	48-hour EC_{50}	1.8 µg/L	USEPA, 2006b
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, 2006b
Claasenia sabulosa	96-hour LC_{50}	2.8 µg/L	USEPA, 2006b
Hydropsyche sp.	96-hour LC_{50}	5.0 µg/L	USEPA, 2006b
Lestes congener	96-hour LC_{50}	10.0 µg/L	USEPA, 2006b
Paleomenetes kadiankesis	96-hour LC_{50}	12.0 µg/L	USEPA, 2006b
Orconectes nais	96-hour LC_{50}	180.0 µg/L	USEPA, 2006b
Penaeus duorarum	48-hour LC_{50}	180.0 µg/L	USEPA, 2006b
Atherix variegata	96-hour LC_{50}	385 µg/L	USEPA, 2006b
Crassostrea virginica	96-hour LC_{50}	>1,000 µg/L	USEPA, 2006b
Callinectes sapidus	48-hour LC_{50}	>1,000 µg/L	USEPA, 2006b
Asellus brevicaudus	96-hour LC_{50}	3,000 µg/L	USEPA, 2006b
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

Appendix B. Risk Estimates of Potential Dermal and Inhalation Exposures during Mixing and Loading for Workers

Equations:

Dermal Dose = (Application Rate x Area Treated x Dermal Unit Exposure (DUE) x Conversion Factor (CF)) / Body Weight (BW)

Inhalation Dose = (Application Rate x Area Treated x Inhalation Unit Exposure (IUE) x Conversion Factor (CF)) / Body Weight (BW)

Dermal Hazard Quotient (DHQ) = Dermal Dose/Reference Dose (RfD)

Inhalation Hazard Quotient (IHQ) = Inhalation Dose/Reference Dose (RfD)

Assumptions for risk estimation:

Input Parameters		Values	Sources
Application Rate (lb a.i./acre)	Maximum	0.62	USDA APHIS, 2015b[1]
	Average	0.31	
Area treated (acre/day)		100	USDA APHIS, 2015b[2]
DUE (µg/lb a.i.)		37.6	USEPA, 2016f[3]
IUE (µg/lb a.i.)		0.219	USEPA, 2016f[4]
CF (mg/µg)		0.001	
BW (kg)		69	Body weight for women
Dermal Dose (mg/kg-day)		9.6E-05	Calculated
		2.6E-04	Calculated
Inhalation Dose (mg/kg-day)		1.9E-05	Calculated
		5.1E-05	Calculated
RfD (mg/kg-day)		0.1	USEPA, 2015
RfD (mg/kg-day)		0.1	USEPA, 2015
DHQ	Maximum	0.3	Calculated
	Average	0.2	Calculated
IHQ	Maximum	0.002	Calculated
	Average	0.001	Calculated
Combined HQ (DHQ + IHQ)	**Maximum**	**0.3**	Calculated
	Average	**0.2**	Calculated

Notes:

1 Maximum application rate: 0.62 lb a.i. per acre for APHIS conventional rate, and Average application rate: 0.31 lb a.i. per acre for APHIS RAATs rate.

2 Assumed the program application of 1000 acre per day.

3 Single layer, gloves PPE levels for the mixing/loading liquids exposure scenario.

4 No respirator PPE level for the mixing/loading liquids exposure scenario.