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

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EXECUTIVE SUMMARY

The United States Department of Agriculture (USDA), Animal and Plant Health Inspection Service (APHIS), Plant Protection and Quarantine (PPQ) is proposing the use of the organophosphate insecticide, naled, in traps or bait stations in its cooperative exotic fruit fly eradication program. DIBROM® 8 Emulsive, is the proposed formulation used in traps and is a liquid containing 62% naled. The Dibrom® Concentrate formulation is used in bait stations in California and Florida and is a liquid containing 87.4% naled. The formulations are restricted use due to eye and skin hazards. They are used only by certified applicators, or persons under their direct supervision, and only for those uses covered by the certified applicator's certification.

USDA-APHIS evaluated the potential human health and ecological risks from the proposed uses of the DIBROM® 8 Emulsive and Dibrom® Concentrate and determined that risks to human health and the environment are negligible. The lack of risk to human health and the environment is based on the low probability of exposure to humans and the environment, and favorable environmental fate and effects data. The proposed application methods (traps or bait stations), and adherence to label requirements, substantially reduces the potential for exposure to humans and the environment, including fish and wildlife. Adverse health risks to workers are not expected based on the application method and low potential for exposure when applied according to label directions. The quantitative evaluation to workers from accidental exposure during mixing did not exceed levels of concern. Adverse health risks to the general public are not expected based on the requirements for public notification as specified on the label, and the placement of traps out of the normal reach of children.

Off-site transport of naled from the proposed applications are minimized by the application method (traps or bait stations) and environmental fate (rapid degradation) of the product. Risk to non-target fish and wildlife is minimal based on the targeted method of application, where the product is applied, and the environmental fate and toxicity profile of naled.

1.0 INTRODUCTION

This human health and ecological risk assessment (HHERA) provides a qualitative and quantitative evaluation of the potential risks and hazards to human health, non-target fish, and wildlife as a result of exposure to the organophosphate (OP) insecticide, naled, under the proposed applications to eradicate various species of exotic fruit flies (e.g., Oriental fruit fly, Guava fruit fly) that enter the United States. The OPs are a group of related pesticides that affect the function of the nervous system.

The methods used in this HHERA 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 U.S. Environmental Protection Agency, Office of Pesticide Programs (USEPA/OPP). The methods used to assess potential ecological risk to non-target fish and wildlife follow USEPA and other published methodologies regarding eco-risk assessment, 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), then a toxicity assessment (the dose-response assessment), and an exposure assessment (identifying potentially exposed populations and determining potential exposure pathways for these populations). In the fourth section (risk characterization) the information from the exposure and toxicity assessments are integrated to characterize the risk of naled use to human health and the environment.

2.0 PROBLEM FORMULATION

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

Naled is an OP insecticide that is in a group of related pesticides that affect the nervous system. Naled is a potent cholinesterase (ChE) inhibitor causing reversible inhibition of erythrocyte acetylcholinesterase and plasma butyryl ChE (USEPA, 2008a). Acetylcholinesterase is an enzyme necessary for the degradation of the neurotransmitter acetylcholine (ACh) and subsequent cessation of synaptic transmission. Inhibition of these enzymes results in the accumulation of ACh at cholinergic nerve endings and continual nerve stimulation, resulting in insect death. Naled degrades to dichlorvos (DDVP), which is another OP insecticide with an identical mode of action. DDVP is used in pest strips in traps in the exotic fruit fly program. A separate HHERA for DDVP is located on the Program's website (https://www.aphis.usda.gov/aphis/ourfocus/planthealth/plant-pest-and-disease-programs/pests-and-diseases/fruit-flies/ct_fruit_flies_home).

Naled is primarily used to control adult mosquitoes but is also registered to control blackflies and leaf-eating insects on a variety of fruits, vegetables, and nuts (USEPA, 2002). The USDA-APHIS exotic fruit fly eradication program uses naled in traps or bait stations to kill exotic fruit flies.

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

2.1 Chemical Description and Product Use

Naled (CAS No. 300-76-5, $C_4H_7O_4PBr_2Cl_2$) is the common name of chemical 1,2-dibromo-2,2-dichloroethyl dimethyl phosphate (figure 2-1).

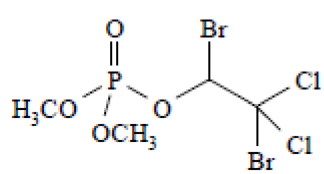


Figure 2-1. The chemical structure of naled

First registered with USEPA in 1959, naled is the active ingredient (a.i.) in the DIBROM® formulation (USEPA, 2002). USDA-APHIS is proposing to use the DIBROM® 8 Emulsive formulation (EPA Reg. No. 5481-479) (AMVAC, 2013) and the Dibrom® Concentrate formulation (EPA Reg. No. 5481-480) (AMVAC, 2014) in the fruit fly program. DIBROM® 8 Emulsive contains 7.5 pounds (lbs) naled per gallon (62.0% naled and 38.0% inert ingredients). Dibrom® Concentrate contains 13.2 lbs naled per gallon (87.4% naled and 12.6% inert ingredients). The DIBROM® 8 Emulsive and Dibrom® Concentrate formulations are restricted use pesticides due to eye and skin hazards. They are used only by certified applicators, or persons under their direct supervision, and only for those uses covered by the certified applicator's certification. The DIBROM® 8 Emulsive product label (AMVAC, 2013) also specifies it is not for use in, and around, residential areas except when used by Federal, State, Tribal, or local government officials responsible for area-wide public health pest or vector control. USDA-APHIS use of the products in or near residential area for fruit fly eradication is in compliance with requirements of the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) Section 24(c) Special Local Need (SLN) labels. USDA-APHIS applications will be made in accordance with label directions for DIBROM® 8 Emulsive, the DIBROM® 8 Emulsive SLN label for California (SLN No. CA-090011) (CDPR, 2013), the Dibrom® Concentrate SLN label for California (SLN No. CA-860005) (California Department of Pesticide Regulation. 2007), and the FIFRA Section 18 emergency exemption for Florida (File Symbol: 16-FL-07) (Florida Department of Agriculture and Consumer Services, 2016).

2.2 Physical and Chemical Properties

Naled is a white solid with a melting point of 27 Celsius (°C) and a vapor pressure of 2 $x10^{-4}$ millimeter of mercury (mm Hg) at 20 °C or 2 x 10^{-3} torr, suggesting it can volatilize into the atmosphere. The Henry's Law constant for naled is 6.5 x 10^{-5} atmosphere $meter^3$/mole at 25 °C. The log octanol/water partition coefficient (log Kow) for naled is 1.4. Naled has low solubility in water (1 milligram per liter (mg/L)) and limited solubility in aliphatic solvents, but it is highly soluble in oxygenated solvents (ketones and alcohols) (USEPA, 2002, 2008a). The DIBROM® 8 Emulsive and Dibrom® Concentrate formulations are an off-white to straw yellow liquid with a sharp, pungent odor. Vapor density is heavier than air with a vapor pressure of 10 mm Hg at 100 °F (37.8 °C). Bulk density values range between 14.97 and 15.28 lb/gallon while specific gravity values range between 1.794 and 1.831 at 20 °C/4 °C (AMVAC, 2015a, b).

2.3 Environmental Fate

The environmental fate describes the processes by which naled 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.

Naled degrades quickly to DDVP and dichloroacetic acid (DCAA) in the environment via chemical hydrolysis and biodegradation. Three field dissipation studies show that naled dissipates rapidly with half-lives of less than two days under terrestrial, aquatic, and forestry field conditions (USEPA, 1997). The dissipation is also rapid for DDVP. The presence of sunlight accelerates degradation with photolysis half-lives of 0.4 days (soil) and 4.4-4.7 days (aqueous) (USEPA, 2008b).

Soil microbes degrade naled with a reported aerobic soil half-life of 1 day (USEPA, 2008b). Naled released to the soil has moderate mobility based on reported Koc values (180-344). Naled and its associated degradates are potentially mobile in soil (less mobile in clay-rich soil), however, they are unlikely to move to surface or groundwater due to the method of application and favorable environmental fate properties such as rapid degradation and low water solubility. Naled is susceptible to degradation in the aquatic environment with short half-lives under various pathways: hydrolysis (half-lives of 4 days (pH 5), 0.642 days (pH 7), and 0.067 days (pH 9)), biodegradation (anaerobic aquatic half-life range of 0.2 to 4.5 days), and photolysis (aqueous half-lives of 4.4-4.7 days) (USEPA, 2008b). Spray drift and direct application for mosquito abatement are the main sources of surface water contamination (USEPA, 2002). These routes of exposure to surface water will not occur for the proposed naled use in the exotic fruit fly program.

The bioaccumulation potential for naled and DDVP are expected to be low based on the log Kow of 1.4 (naled) and 1.6 (DDVP) (USEPA, 2008a), and an estimated bioconcentration factor (BCF) of 0.4 (naled), and measured BCFs of <0.5 and 0.8 (DDVP) (NIH, 2016a, b). Plants remove bromide from naled to form DDVP, which may evaporate or be further metabolized.

2.4 Hazard Identification

Naled is a hazard to human health due to severe acute eye irritation, corrosive dermal irritation, and neurotoxicity (USEPA, 2002). Naled causes contact sensitization dermatitis including residual papular dermatitis on the arm, glazing on the skin of the cheek, mild irritation of the neck skin, and a maculopapular eruption of the abdomen. For example, dermatitis was observed by an individual picking flowers sprayed with naled, and by an aerial applicator who had used naled (NIH, 2016a).

2.4.1 Toxicological Effects

Similar to other OP pesticides, naled is a ChE inhibitor. Symptoms of ChE inhibition in humans include nausea, dizziness, and confusion. Exposure to high doses of naled, which could occur during an accident or major spill, can result in respiratory paralysis and death.

2.4.2 Absorption, Distribution, and Excretion

Naled is rapidly absorbed through all normal routes of exposure (mucous membrane of digestive system, respiratory system, and skin), and conveyed by the blood to various body tissues. Metabolism occurs in the liver. Metabolites of naled include DDVP and hydrolysis products, such as methyl phosphates (mono- and di-), desmethyl DDVP, and inorganic phosphate

(USEPA, 1999). Naled residues were non-detectable (< 0.01 ppm) in milk from Holstein cows subject to body and premise sprays for 14 days using an emulsifiable concentrate formulation (NIH, 2016a).

2.4.3 Human Incidents

USEPA conducted a human poisoning incident review of the USEPA/OPP incident data system (IDS) for naled exposures (USEPA, 2008c). The IDS review reported two human incidents related to naled (Dibrom® Concentrate) that occurred in 2002 and 2005. USEPA considered both human incident reports as moderate with health symptoms in one incident as throat irritation, bronchospasm, agitation/irritability, and confusion, and the other incident reported nausea and headache.

2.4.4 Acute Toxicity

The technical a.i. of naled has moderate acute toxicity (Category II) via oral, dermal, and inhalation exposure routes. The oral median lethality (LD_{50}) values in rats are 92 mg/kg (females) and 191 mg/kg (males) (administered in carboxymethyl-cellulose), and 230 mg/kg (females) and 325 mg/kg (males) (administered in corn oil). The dermal LD_{50} values in rabbits are 360 mg/kg (female) and 390 mg/kg (male). The inhalation LC_{50} values in rats are 0.19 mg/l (females) and 0.20 mg/l (males) in 4-hour exposures. For eye and dermal irritation, naled has high acute toxicity (Toxicity Category I) causing severe eye irritation and corrosive dermal irritation. Naled was weakly positive in dermal sensitization tests using the guinea pig (USEPA, 2009).

The DIBROM® 8 Emulsive formulation safety data sheet reported an acute oral LD_{50} of 235 mg/kg in rats (Category II), an acute dermal LD_{50} of 5,050 mg/kg in rabbits (Category IV), and an acute inhalation LC_{50} of 1.51 mg/l in a 4 hour exposure using male rats (Category III) (AMVAC, 2015a). The DIBROM® 8 Emulsive formulation is corrosive to skin and extremely irritating to the eye, which causes severe skin burns and serious eye damage. However, the formulation is not a skin sensitizer, and is less toxic for inhalation and dermal routes compared to technical naled.

The Dibrom® Concentrate formulation safety data sheet reports an acute oral LD_{50} of 50 to 500 mg/kg and an acute dermal LD_{50} of 4,037 mg/kg for naled technical, and an acute inhalation LC_{50} value of 1.51 mg/l in male rats for DIBROM® 8 (AMVAC, 2015b). The Dibrom® Concentrate formulation is corrosive to the skin and eye, causing mild skin irritation and serious eye damage. The formulation is a weak skin sensitizer.

2.4.5 Subchronic and Chronic Toxicity

A 28-day subchronic oral toxicity study in rats reported a No Observed Adverse Effect Level (NOAEL) of 1.0 mg/kg/day, and a Lowest Observed Adverse Effect Level (LOAEL) of 10 mg/kg/day based on cholinergic signs, and plasma and brain ChE inhibition. USEPA used this study to develop an acute oral reference dose (RfD) (see Section 3 for further discussion) (USEPA, 2001).

A 28-day dermal toxicity study in rats reported a NOAEL of 10 mg/kg/day, and a LOAEL of 20 mg/kg/day (within 10 days of exposure) based on brain ChE inhibition in females, and plasma and red blood cell ChE inhibition in males and females. This study also reported a systemic NOAEL of 10 mg/kg/day and a systemic LOAEL of 40 mg/kg/day based on minimal kidney effects (USEPA, 2001).

A 90-day inhalation study in rats reported an inhalation NOAEL of 0.23 µg/L (0.053 mg/kg/day), and a LOAEL of 1.29 µg/L (0.298 mg/kg/day) based on plasma and red blood cell ChE inhibition. The study also reported a systemic NOAEL of 1.29 µg/L and a systemic LOAEL of 5.8 µg/L based on clinical signs of toxicity (USEPA, 2001).

A 1-year oral toxicity study using dogs reported a NOAEL of 0.2 mg/kg/day and a LOAEL of 2 mg/kg/day based on plasma and red blood cell ChE inhibition, and decreased hematocrit and hemoglobin values in both male and female dogs (USEPA, 2001).

The 2-year chronic oral toxicity study in rats reported a NOAEL of 0.2 mg/kg/day and a LOAEL of 2 mg/kg/day based on inhibition of brain ChE activity. USEPA used this study to develop a chronic oral RfD (see Section 3 for further discussion) (USEPA, 2001).

2.4.6 Nervous System Effects

The acute oral neurotoxicity study in rats administered doses of 0, 25, 100, or 400 mg/kg reported a NOAEL of 25 mg/kg for males, and a LOAEL of 100 mg/kg for males based on clinical signs of neurotoxicity (convulsions, tremors, increased secretions, exophthalmos, respiratory changes, reduced muscle strength, and slowed response to stimuli). This study did not identify a NOAEL for females. The estimated NOAEL and LOAEL for females were 5 mg/kg and 25 mg/kg, respectively, based on minimal neurological effects at 25 mg/kg in the main study, and no toxicity at 5 or 15 mg/kg in a preliminary range-finding study (USEPA, 1999).

The 90-day subchronic oral neurotoxicity study in rats that administered doses of 0, 0.4, 2.0, or 10.0 mg/kg/day reported a NOAEL of 2.0 mg/kg/day (female) and 10.0 mg/kg/day (males). Minimal neurological effects observed in three out of ten of the high dose females included sporadic occurrence of tremors (forelimb, hindlimb and/or whole body) (USEPA, 1999).

2.4.7 Reproductive or Developmental Effects

A two-generation reproductive study using naled and rats (0, 2, 6 or 18 mg/kg/day by gavage) reported a NOAEL of 6 mg/kg/day for parental systemic effects and a LOAEL of 18 mg/kg/day based on a decrease in weight gain in both generations. The reproductive toxicity NOAEL was

18 mg/kg/day (the high dose tested). This study did not show increased sensitivity to naled, and there was no clinical evidence of behavioral alterations in young rats compared to adults (USEPA, 1999, 2002).

A developmental toxicity study using naled and pregnant rats (0, 2, 10, or 40 mg/kg/day by gavage) reported a NOAEL of 10 mg/kg/day for maternal toxicity and a LOAEL of 40 mg/kg/day based on clinical signs (tremors, hypo-activity, discharge from the mouth and eyes, and difficult breathing), and reduced weight gain. The developmental toxicity NOAEL was 40 mg/kg/day (the high dose tested). The developmental toxicity study using artificially inseminated rabbits (0, 0.2, 2, or 8 mg/kg/day by gavage) reported a NOAEL of 8 mg/kg/day for maternal and developmental toxicity. The developmental rat and rabbit toxicity studies did not show increased sensitivity to the fetus compared to maternal animals following acute *in utero* exposure to naled. There was also no evidence of abnormalities in the development of the fetal nervous system (USEPA, 1999, 2002).

2.4.8 Carcinogenicity and Mutagenicity

USEPA classifies naled as a “Group E – Evidence of Non-carcinogenicity for Humans” pesticide based on the lack of evidence of carcinogenicity in mice (89-week carcinogenicity study) and rats (two-year carcinogenicity study) (USEPA, 2015a, 2001). USEPA classifies the degradation product DDVP as “suggestive evidence of carcinogenicity, but not sufficient to assess human carcinogenic potential” (USEPA, 2015a, 2006).

Naled is not mutagenic based on an *in vivo* gene mutation study on mouse spots in pregnant mice, a gene mutation assay in *Salmonella* (Ames assay), the DNA damage test in bacteria, a cytogenetic effects *in vivo* in the mouse bone marrow micronucleus assay, and an *in vivo* cytogenetics study in rats (USEPA, 2001).

2.4.9 Endocrine System Effects

Naled is on the list of Endocrine Disruptor Screening Program (EDSP) universe of chemicals for potential endocrine disruptor screening and testing (USEPA, 2012a). The list is not a list of “known” or “likely” endocrine disrupting chemicals (USEPA, 2012b). Naled was screened as a pesticide a.i. using the ToxCast "Endocrine Receptor Model" for estrogen receptor bioactivity and showed negative results (USEPA, 2015b).

2.4.10 Immune System Effects

The USEPA registration review of naled did not address immune system effects (USEPA, 2001). A literature review did not identify any naled mammalian immunotoxicity studies. USEPA requested an immunotoxicity test (870.7800) in its Data Call-In Response for registration review (USEPA, 2010). The results of that study reported a NOAEL of 10 mg/kg/day, the highest dose tested (USEPA, 2012c). USEPA concluded that naled does not directly target the immune system based on overall weight of evidence. The study did report a systemic NOAEL of 0.4 mg/kg/day and a LOAEL of 2 mg/kg/day based on reduced erythrocyte and brain AChE activity.

2.4.11 Toxicity of Other Ingredients

Approximately 38.0% of the DIBROM® 8 Emulsive formulation and 12.6% of the Dibrom® Concentrate formulation contains inert ingredients, such as petroleum distillates (AMVAC, 2013, 2014). The AMVAC Chemical Corporation safety data sheets (2015a, b) indicate the DIBROM® 8 Emulsive and the Dibrom® Concentrate formulations contain <2% and <1% of naphthalene, and ≤0.3 % and ≤0.4% of DDVP in impurities. Naphthalene is a potential human carcinogen (NTP, 2014). DDVP is the degradation product of naled, another registered OP insecticide used in the program, with the same mode of action as naled. A separate risk assessment has been prepared for DDVP. Comparative acute oral, dermal, and inhalation toxicity values for the technical a.i. and the Dibrom® Concentrate formulation show that the formulation has lower toxicity.

The use of naled in the program may also include fruit fly attractants or carriers that increase efficacy and reduce exposure to human health and the environment.

Methyl eugenol is a chemical attractant used to attract fruit flies. Methyl eugenol is a naturally occurring constituent found in a number of plants such as nutmeg, pimento, lemongrass, tarragon, basil, star anise and fennel (European Commission, 2001). USEPA's Tolerance Reassessment Eligibility Document for methyl eugenol concluded "...there is a reasonable certainty that no harm to any population or subgroup will result from the dietary and water exposure to methyl eugenol from uses specified in the existing exemption for the requirements for tolerance for methyl eugenol under 40 CFR §180.1067." (USEPA, 2006). The Food and Drug Administration classifies methyl eugenol as a “Generally Recognized as Safe” compound suggesting a low hazard to human health.

Cuelure is another chemical attractant. Cuelure is 4-(p-Acetoxyphenyl)-2-butanone (CAS No. 3572-06-3) and has low acute toxicity with an oral LD_{50} of 3,038 mg/kg (rat), inhalation LC_{50} of >2,800 mg/m^3 (rat), and dermal LD_{50} of >2,025 mg/kg (rabbit) (ChemlDplus, 2016).

Min-U-Gel is a thickener and carrier used to dispense a small dollop of naled and an attractant to inanimate objects such as telephone poles. Acute toxicity data is unavailable, however, prior to mixing Min-U-Gel, it is a mineral dust form that may cause respiratory effects through prolonged or repeated exposure (Active Mineral International, LLC, 2017).

3.0 DOSE-RESPONSE ASSESSMENT

3.1 Human Health Dose-Response Assessment

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

The USEPA/OPP developed an oral RfD of 0.01 mg/kg/day for an acute exposure scenario for the general population including infants and children (USEPA, 2009). The acute RfD for naled was derived by applying an uncertainty factor of 100 (10x for interspecies extrapolation, 10x for intraspecies variation, and 1x Food Quality Protection Act safety factor) to the NOAEL of 1.0 mg/kg/day from the 28-day oral toxicity study in rats (USEPA, 1999).

The USEPA/OPP also derived a chronic RfD of 0.002 mg/kg/day for a chronic dietary exposure scenario for all populations (USEPA, 2009). The chronic RfD for naled was developed by applying an uncertainty factor of 100 to the NOAEL of 0.2 mg/kg/day from the chronic oral study in rats (USEPA, 1999).

USEPA concluded that naled is moderately absorbed through the skin at peak levels of 21–23% after 10–24 hours of exposure (USEPA, 2001). A dermal absorption factor of 21% for a 10-hour exposure period represents a normal worker day scenario.

The USEPA/OPP did not derive a cancer potency factor because of the classification of naled as showing “evidence of non-carcinogenic to humans”.

The USEPA established tolerances for the combined residues of naled and its degradate DDVP (expressed as naled) resulting from the application of the pesticide to growing crops, or from direct application to livestock and poultry (40 CFR 180.215). The tolerance levels of some fruits are 3 ppm for grapefruit, lemon, orange, and tangerine, 1 ppm for strawberry, and 0.5 ppm for grape, melon, and peach (USEPA, 2009).

3.2 Ecological Dose-Response Assessment

3.2.1 Wild Mammal, Avian and Reptile Toxicity

The acute and chronic toxicity of naled to mammals is characterized in section 2.4 of this risk assessment. Additional wild mammal studies include an oral LD_{50} study using the mule deer (LD_{50} ~ 200 mg/kg) (Hudson et al., 1984). Naled is classified as moderately toxic in oral, inhalation, or dermal acute exposures for mammals.

Acute oral toxicity studies for birds show that naled is moderately toxic with median lethality values ranging from 36.9 to 120 mg/kg (table 3-1).

Table 3-1. Median oral lethality values for naled and various bird species.

Test Organism	LD_{50} (mg/kg)	Reference
Mallard, *Anas platyrynchus*	52.2	Hudson et al., 1984
Canada goose, *Branta canadensis*	36.9	USEPA, 1997
Sharp-tailed grouse, *Tympanuchus phasianellus*	64.9	Hudson et al., 1984
Pheasant, *Phasianus colchicus*	120	Hudson et al., 1984

Naled subacute toxicity in dietary studies is considered slight with median dietary lethality values ranging from 1,327 mg/kg for the Japanese quail to 2,724 mg/kg for the mallard (table 3-2).

Table 3-2. Median dietary lethality values for naled and various bird species.

Test Organism	LC_{50} (mg/kg)	Reference
Mallard, *Anas platyrynchus*	2,724	USEPA, 1997
Japanese quail, *Coturnix japonica*	1,327	USEPA, 1997
Pheasant, *Phasianus colchicus*	2,538	USEPA, 1997
Bobwhite quail, *Coturnix virginianus*	2,117	USEPA, 1997

Chronic avian toxicity data for naled does not appear to be available based on a search of the literature.

A review of the literature did not indicate any available reptile toxicity data testing using naled. In their ecological risk assessment process for pesticides, USEPA assumes comparative sensitivity between reptiles and birds. There is uncertainty in this assumption because reptiles and birds have different physiology and life histories; however, in cases where no data is available reptile toxicity is assumed comparable to avian toxicity data.

The primary metabolite of naled, DDVP has comparably higher toxicity than the parent compound for mammals and birds. The effects and risk of DDVP use in the exotic fruit fly program are discussed further in a separate HHERA.

3.2.2 Terrestrial Invertebrate Toxicity

Naled is considered highly toxic to terrestrial invertebrates, including pollinators. The contact toxicity value for the honey bee (*Apis mellifera*) is high with a reported 48-hour LD_{50} value of

0.48 micrograms (µg) a.i./bee (USEPA, 1997). Toxicity is also high for other bee species such as the alfalfa leafcutter bee (*Megachile rotundata*) and alkaline bee (*Nomia melanderi*). Concentrations required to reach an LC_{50} were 0.0245 µg/bee for *M. rotundata* and 0.0016 µg/bee for *N. melanderi* (Torchio, 1973). Bargar (2012) reported acute contact toxicity values ranging from 2.3 to 7.6 µg/g for adult butterfly species (great southern white (*Ascia monuste*), common buckeye (*Junonia coenia*), painted lady (*Vanessa cardui*), and julia butterflies (*Dryas julia*)). *Ascia monuste* was the most sensitive test species while *D. julia* was the least sensitive. Hoang et al. (2011) also reported high acute contact toxicity to larval and adult butterflies including the atala hairstreak (*Eumaeus atala*), common buckeye (*Junonia coenia*), zebra longwing (*Heliconius charitonius*), and white peacock (*Anartia jatrophae*). Toxicity values ranged from 0.45 to 1.1 µg/g for fifth instar larvae and from 0.19 to 28.22 µg/g for adult butterflies. The sensitivity of pollinators such as bees and butterflies have also been validated in field studies using liquid broadcast applications of naled at labelled application rates (Torchio, 1983; Zhong et al., 2010). However, these types of applications are not proposed for the exotic fruit fly program and are not relevant for this analysis.

3.2.3 Terrestrial Plant Toxicity

No data appear to be available in the literature regarding the effects of DDVP to terrestrial plants. Toxicity would be expected to be low in cases where exposure could occur due to the mechanism of action of DDVP and the proposed formulation, which would eliminate the potential for significant exposure.

3.2.4 Aquatic Vertebrates Toxicity

Naled is moderately to highly toxic to fish depending on the test species (table 3-3). Cold-tolerant freshwater species such as trout are more sensitive to naled compared to warm freshwater species such as bass, bluegill, and catfish. Marine species also appear to be more tolerant of naled when compared to cold water species such as trout.

Table 3-3. Acute naled toxicity data for freshwater and marine fish species.

Test Organism	**LC_{50} (mg/L)**	**Reference**
Lake trout, *Salvelinus namaycush*	0.087	USEPA, 1997
Cutthroat trout, *Oncorynchus clarkii*	0.127	USEPA, 1997
Channel catfish, *Ictalurus punctatus*	0.710	USEPA, 1997
Bluegill, *Lepomis macrochirus*	2.2	USEPA, 1997
Rainbow trout, *Oncorynchus mykiss*	0.160-0.345	USEPA, 1997
Sheepshead minnow, *Cyprinodon variegatus*	1.2	USEPA, 1997
Largemouth bass, *Micropterus salmoides*	1.9	USEPA, 1997
Fathead Minnow, *Pimephales promelas*	3.3	USEPA, 1997

Chronic exposure studies are limited to an early life stage study using the fathead minnow, *Pimephales promelas* (USEPA, 1997). The No Observable Effect Concentration (NOEC), Lowest Observable Effect Concentration (LOEC), and maximum allowable toxicant concentration were reported as 6, 10, and 15 µg/L, respectively. The most sensitive endpoint in the study was impaired growth.

Available acute toxicity data for amphibians show naled sensitivity to be comparable to warm water fish effects. Sanders (1970) reported a 96-hour median lethality value of 1.7 mg/L for the western chorus frog, *Pseudacris triceratus*.

3.2.5 Aquatic Invertebrates

Naled is considered highly toxic to most aquatic invertebrates (table 3-4). Freshwater cladocerans are the most sensitive test species with median effective concentration (EC_{50}) values of less than 0.5 µg/L while the eastern oyster is the least sensitive with a reported EC_{50} value of 190 µg/L (table 3-4).

Table 3-4. Acute naled toxicity for various freshwater and marine invertebrates.

Test Organism	EC/LC_{50} (µg/L)	Reference
Cladoceran, *Daphnia pulex*	0.4	USEPA, 1997
Cladoceran, *Daphnia magna*	0.3	USEPA, 1997
Cladoceran, *Simocephalus serrulatus*	1.1	USEPA, 1997
Stonefly, *Pteronarcys californica*	8.0	USEPA, 1997
Amphipod, *Gamarus fasciatus*	18	USEPA, 2007
Mysid, *Americamysis bahia*	8.8	USEPA, 2007
Eastern oyster, *Crassostra virginica*	190	USEPA, 2007

Chronic studies using naled and aquatic invertebrates are limited to a 21-day life cycle study using the cladoceran, *Daphnia magna* (USEPA, 1997). Length was the most sensitive endpoint with a reported NOEC of 0.98 µg/L. The Maximum Allowable Toxicant Concentration and LOEC were reported as 0.13 and 0.18 µg/L.

3.2.6 Aquatic Plants

Aquatic plant testing using naled shows low toxicity to the aquatic macrophyte, *Lemna gibba*, with a NOEC of greater than 1.8 mg/L. The freshwater diatom, *Navicula pelliculosa*, was the most sensitive test organism with a reported 5-day EC_{50} value of 0.025 mg/L (table 3-5).

The primary metabolite of naled in aquatic systems is DDVP, which is a registered insecticide that is also currently used in the exotic fruit fly program. The ecological effects of DDVP are discussed in a separate HHERA. In general, DDVP has greater toxicity to aquatic organisms when compared to naled but is dependent on the test species. Available formulation data for naled suggest comparable toxicity to aquatic organisms. Muncy and Oliver (1963) reported a 72-hour median threshold level of 4.0 mg/L for the crayfish, *Procambarus clarkii*. Maki et al. (1973) reported 24-hour LC_{50} values of 6.8 mg/L and 11.4 µg/L for the hellgrammite, *Corydalus cornutus,* and stonefly, *Hydroperla crosbyi*, respectively. USEPA (1997) also showed comparable or less toxicity for various naled formulations when compared to the technical grade naled for the eastern oyster, sheepshead minnow, rainbow trout, and bluegill.

Table 3-5. Aquatic plant toxicity for naled.

Test Organism	**EC_{50} (mg/L)**	**Reference**
Anabaena flos-aque	0.91	USEPA, 2007
Skeletonema costatum	0.049	USEPA, 2007
Navicula pelliculosa	0.025	USEPA, 2007
Lemna gibba	≥ 1.8*	USEPA, 2007
Selenastrum capricornutum	0.037	USEPA, 2007

*No observable effect concentration

4.0 EXPOSURE ASSESSMENT

4.1 Human Health Exposure Assessment

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

4.1.1 Identification of Potentially Exposed Human Populations and Complete Exposure Pathways

APHIS uses naled in traps or as spot treatments to eradicate exotic fruit fly pests. Based on the SLN label requirements for the traps, DIBROM® 8 Emulsive is diluted to 25% a.i. with an approved lure for eradication trapping (42 ounces (oz.) of product mixed with 86 oz. of attractant for one gallon). Approximately 5 ml of diluted material is applied to absorbent wicks using calibrated equipment (e.g., a dropper, syringe, or a bottle top dispenser). The traps are rebaited monthly. The traps are placed at approximately 1,000 traps per square mile in a 1.5 mile radius from each fruit fly detection site on tree trunks and limbs.

Spot treatments are a gel-like mixture of an attractant such as methyl eugenol or cuelure, an insecticide such as naled, and a carrier such as Min-U-Gel that is applied as a dollop to objects such as utility poles and trees at heights that are out of reach of children and pets. In California, an approximately 5 ml volume of material is applied as a spot treatments (California Department of Pesticide Regulation, 2007). The material is a mixture of 19 fluid oz. of Dibrom® Concentrate in each gallon of an approved attractant, and ordinarily 2 to 3 lbs of the carrier Min-U-Gel. The spot applications are applied up to 600 spot treatments per square mile on telephone or light poles, tree-trunks and limbs, or other inanimate objects using hand spray equipment only. Applications are repeated every two to four weeks.

For spot treatments in Florida, 3 ml to 10 ml of formulated mix per station is applied to utility poles, tree trunks, and other inanimate objects at heights which are out of the normal reach of children and pets in non-crop sites (Florida Department of Agriculture and Consumer Services, 2016). The formulated mixture is a ratio of 1.7 ounces of naled to 12.7 ounces of methyl eugenol or cuelure adding Min-U-Gel as a thickener and carrier ingredient to obtain the desired consistency. Up to 600 spot treatments per square mile will be applied around each exotic fruit fly detection site every 1 to 4 weeks, depending on air temperature.

Workers in the program are the most likely human population segment to be exposed to naled based on the proposed application method for naled. Occupational exposure to naled may occur through inhalation and dermal contact during the application (mixing and applying). However, direct contact exposures are minimized with the use of personal protective equipment (PPE) as further discussed in the next section. Drift from applications will not occur based on how naled is applied to traps and bait stations.

The general public (e.g., residents) is not recognized as a potentially exposed population group due to public notification about exotic fruit fly eradication activities and the method of application that would eliminate off-site movement of naled via drift or runoff. USDA-APHIS notifies residential property owners about traps on their properties to reduce the potential for exposure.

A complete exposure pathway associated with direct contact to naled from traps or spot treatments applications is not identified for the general public. Based on the USDA-APHIS use pattern in the exotic fruit fly eradication program, the potential for the general public to be exposed to naled is not expected via inhalation of ambient air, ingestion of food and drinking water, or dermal contact. Volatilization of naled occurs in traps and spot treatments; however, the exposure potential is low due to the small quantities that are used in the trap and baits. The potential exposure to naled in traps or spot treatments through direct contact by a child is not expected because families would be notified of surveys, and the traps or spot applications will be placed out of reach of children. A complete exposure pathway is not identified for dietary consumption of fruit from fruit bearing trees because naled is not applied directly to edible plants.

A complete exposure pathway is not identified for groundwater. The proposed use pattern of naled in traps and as spot treatments suggests that naled would not be transported by drift or runoff in quantities that could threaten drinking water sources, such as groundwater. In addition naled, and associated degradates, are unlikely to leach into groundwater due to low water solubility and rapid degradation (see Section 2.3).

A complete exposure pathway is not identified for surface water. Significant surface runoff is not expected to occur from program applications of naled based on program and label requirements, as well as low water solubility and rapid degradation of naled in the environment.

4.1.2 Exposure Evaluation

This section qualitatively evaluates routine worker exposure and quantitatively evaluates accidental worker exposure from the direct contact through mixing naled for program use.

Direct contact to naled during application is not expected to occur under normal conditions with proper worker hygiene and properly functioning PPE. The labels specify PPE for pesticide applicators that are mixing the product and applying the diluted material to the wicks in traps

(CDPR, 2013) or for use in spot treatment applications (CDPR, 2007). Protection measures include protective eyewear (goggles, face shield, or safety glasses), long-sleeved shirt and long pants, socks plus shoes, and chemical-resistant gloves (barrier laminate, butyl rubber, nitrile rubber, or Viton, selection category E), and an apron when mixing and loading. The engineering controls for mixing and loading include a well-ventilated area (outdoors), or the use of ventilation systems (such as fume hoods, lab hoods, ventilated glove boxes, and exhaust fans for indoors or inside an enclosed structure). Engineering controls are required to capture and direct naled vapors away from the applicator, as well as to ensure naled vapors do not result in exposure to others in the area. When an engineering control is not possible, the label requires a respirator that meets safety standards for removing organic vapors (AMVAC, 2013, 2014). The label-required PPEs for workers include protective eye wear, coveralls over long-sleeve shirt and long pants, chemical-resistant gloves, chemical-resistant footwear plus socks, a chemical-resistant apron if exposed to the concentrate, chemical-resistant headgear for overhead exposure, and a respirator as specified above.

In the safety data sheets, AMVAC (2015a, b) recommends the use of effective engineering controls to comply with the occupational exposure limits (i.e., Occupational Safety and Health Administration's permissible exposure limits of 3 mg/m^3 (naled), 50 mg/m^3 or 10 ppm (naphthalene), and 1 mg/m^3 (DDVP), and the American Conference of Governmental Industrial Hygienists' time-weighted average (TWA) of 0.1 mg/m3 inhalable fraction and vapor (naled and DDVP) and 10 ppm (naphthalene), and The National Institute for Occupational Safety and Health's TWA of 3 mg/m3 (naled), 50 mg/m3 or 10 ppm (naphthalene), and 1 mg/m^3 (DDVP), and short-term exposure limit of 75 mg/m^3 or 15 ppm (naphthalene)).

Accidental exposure may occur from splash or transfer from contaminated gloves or clothing to an unprotected skin area, such as the face. The occurrence of accidental exposure is unlikely with well-trained certified applicator's adherence to the PPE discussed in the above paragraph, the small amounts (5 ml of diluted material) used in each trap, and the 3 to 10 ml of diluted material used in each spot treatment application. As a conservative approach, the accidental exposure scenario from potential direct contact during mixing is quantified assuming that chemical-resistant gloves leak resulting in dermal exposure, and respirators do not function properly resulting in inhalation exposure, both while using the concentrated formulation.

Unit exposures from the Occupational Pesticide Handler Unit Exposure Surrogate Reference Table (USEPA, 2016b) were used to estimate potential exposure doses for a worker during mixing because chemical-specific data to assess potential exposure to occupational pesticide handlers are not available. These unit exposure values recommended by USEPA for standard occupational pesticide handler exposure scenarios are derived from a number of sources, including the Pesticide Handler Exposure Database, the Outdoor Residential Exposure Task Force, the Agricultural Handler Exposure Task Force, or other available registrant-submitted exposure monitoring studies. Under the exposure scenario for the mixing/loading liquids, the unit exposures are 220 µg/lb a.i. and 0.219 µg/lb a.i. for dermal contact under the single layer (long-sleeve shirt, long pants, shoes plus socks) and no gloves and for inhalation under no respirators

PPE levels, respectively (USEPA 2016b). Per the label directions (AMVAC, 2014), the amount of undiluted DIBROM® concentrate applied to any site must not exceed 2 fl. oz. (0.21 lb of naled a.i.) per acre within a 7-day period for a site, which was used as the daily mixing concentration for a worker. The accidental scenario represents a worst-case exposure scenario. The following equations were used to estimate the exposure dose of direct contact for workers:

Exposure Dose = Daily Dose Rate x Dermal Absorption Factor/Body Weight (Dermal) or Daily Dose Rate/Body Weight (Inhalation)

Daily Dose Rate = Unit Exposure (mg/lb a.i.) x Daily Mixing Concentration (lb a.i./day)

A dermal absorption factor of 21% was applied to the dermal exposure dose estimation. Estimations of exposure doses for naled from dermal and inhalation routes are summarized in table 5-1.

4.2 Ecological Exposure Assessment

4.2.1 Terrestrial Exposure Assessment

The use pattern for naled suggests that exposure to nontarget vertebrates is unlikely to occur. Naled is applied to a wick that is inserted into a trap or is mixed with a carrier and applied directly to inanimate objects. Removal of traps by a scavenging small mammal that could be exposed to naled has not been noted in previous trapping efforts during exotic fruit fly outbreaks. In the case that a small mammal came into contact with the trap it would be highly unlikely that it would consume the wick due to its composition. Inhalation and dermal exposure would also be low because naled is contained within the trap preventing significant exposure. Exposure to naled applied in a carrier agent (Min-U-Gel) to poles and other structures would be slightly more compared to a trap but still very low because vertebrates would not be attracted to those applications.

Non-target terrestrial invertebrate exposure is not quantified because exposure will be primarily to exotic fruit flies due to the use of the trap or naled mixed with a carrier in combination with a fruit fly attractant. Any non-target invertebrate exposure would be incidental and not expected to be significant for any group of terrestrial invertebrates other than the target pest.

4.2.2 Aquatic Exposure Assessment

Aquatic exposure from naled use in the exotic fruit fly eradication program is unlikely. Naled is applied to a wick or carrier by hand and then either inserted into a trap or applied directly to an inanimate object so drift would not be a pathway for aquatic exposure. Runoff also is not a significant exposure pathway because any traps that could fall to the ground would not be expected to be carried as runoff to a receiving water body.

The potential for aquatic exposure from naled use was approximated for a scenario where a trap drops into a water body. This scenario is unlikely; however, a conservative estimate was made so that comparisons could be made to the available effects data. Naled is mixed with attractants and may also be mixed in with a carrier at various concentrations. In this scenario the wick application of naled was used to estimate a potential aquatic residue value. Based on the SLN for use in California, a DIBROM® 8 Emulsive concentration of 25% a.i. with an approved lure for eradication trapping (42 oz of product mixed with 86 oz of attractant for one gallon) was assumed. Approximately 5 ml of diluted material is applied to an absorbent wick. The USEPA standard pond and wetland dimensions were used to estimate naled values in both water bodies. Both water bodies are a square acre with the pond being 6.56 feet deep and the wetland being six inches in depth. Acute instantaneous residues in the wetland and pond habitats ranged from 2.20 to 0.18 µg/L, respectively. The estimates assume uniform distribution of naled in both static water bodies and that no degradation or dissipation of naled would occur once in solution. Estimates for residues in flowing streams and larger water bodies would be much less due to higher dilution rates.

5.0 RISK CHARACTERIZATION

Risks associated with potential adverse effects are characterized qualitatively and quantitatively in this section. Results from the risk characterization suggests that the use of naled for the fruit fly eradication program will pose minimal risks to human health, and ecological risks would be negligible. Fruit fly quarantines of *Bactrocera* are fairly infrequent and usually do not occur every year or in the same location.

5.1 Human Health

Exposure to naled via oral, inhalation, and dermal routes is expected to be minimized by workers' (i.e., certified applicators) adherence to the label-required PPE. Naled is a hazard to humans due to its high acute toxicity causing severe eye irritation and skin corrosiveness as well as its neurotoxicity. The low potential for exposure to naled from the traps and spot treatments applications indicate that adverse risks to workers are not expected.

Accidental exposure of workers from splash to unprotected body areas may occur. The exposure frequency is considered low for this exposure scenario because only certified applicators mix and make applications. Therefore, risk from accidental exposure is expected to be minimal.

To quantify the potential risks to workers from accidental exposure during mixing using the naled concentrate product, estimated potential exposure doses were derived based on conservative assumptions (table 5-1). The accidental risk estimates are based on the daily mixing concentration of the label-allowed 2 fl. oz. of undiluted DIBROM® Concentrate (0.21 lbs a.i.) per acre within a 7-day period for a site. The exposure estimates were then compared to the available acute RfD of 0.01 mg/kg/day for workers to calculate hazard quotient (HQ) values as shown in the following equation:

$$HQ = \text{Exposure Dose}/RfD$$

The estimated HQs for an accidental exposure scenario were 0.01 (dermal) and 0.0001 (inhalation) (table 5-1). The estimated HQs from the potential dermal contact and inhalation of the accidental exposure scenario are below the USEPA acceptable HQ of 1. The risk assessment results show that the estimated risks for the label applications from accidental naled exposure are low.

The dietary risks to the public from exposure to naled are negligible based on notification of the public prior to treatment, and the proposed application methods. The risks associated with residential children being accidentally exposed to naled in traps or bait stations are low because USDA-APHIS placement of traps or baits are out of the normal reach of children.

Table 5-1. Risk estimations for potential accidental exposure during mixing.

Parameters and Equations	Units	Mixing		Sources
		Dermal	Inhalation	
Dose = PDR*DAF/BW (dermal) Dose = PDR/BW (inhalation)	mg/kg-d	1.1E-03	2.3E-04	Calculated
DAF = dermal absorption factor	%	21	NA	USEPA 2001
BW=body weight	kg	80	80	USEPA 2014
PDR = UE * DMC (mg/day)				
PDR =daily dose rates	mg/day	0.090132	0.018241	Calculated
UE = unit exposure	mg/lb a.i.	0.22	0.000219	Unit exposures for the mixing/loading liquids exposure scenario (single layer, no gloves PPE level for dermal and no respirator for inhalation) (USEPA 2016b).
DMC = daily mixing concentration	lb a.i./day	0.21	0.21	The label allowed 2 fl. oz. of undiluted DIBROM Concentrate (0.21 lbs a.i.) per acre within a 7 day period for a site was used for the daily mixing concentration.
RfD = reference dose	mg/kg/day	0.01	0.01	Acute oral RfD, USEPA 2009
HQ = Dose/RfD				
HQ = Hazard Quotient		**0.01**	**0.0001**	Calculated

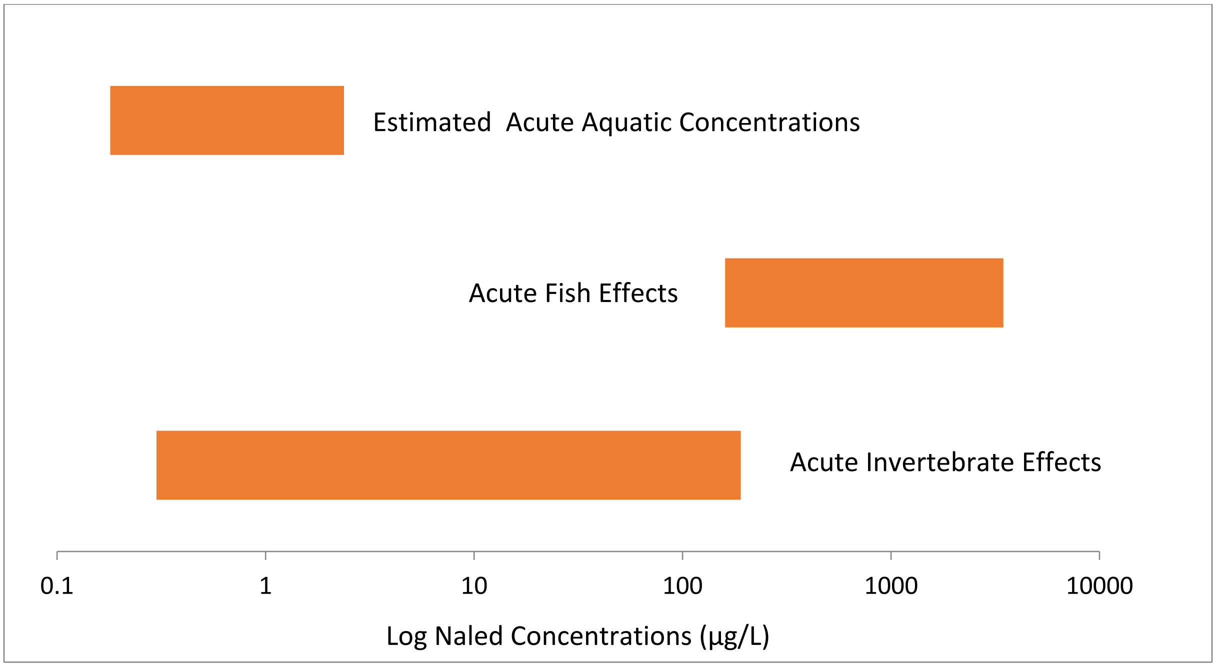
NA – not applicable

5.2 Terrestrial and aquatic risk characterization

The lack of significant exposure to terrestrial vertebrates from naled applications in the exotic fruit fly eradication program suggests negligible risk to this group of non-target organisms. Similarly, there is a lack of significant exposure to most non-target terrestrial invertebrates due to naled use in traps or in a carrier in combination with a fruit fly attractant. Naled is toxic to pollinators such as honey bees and butterflies; however, the lack of significant exposure due to the use pattern reduces the risk to these groups of invertebrates. There is some risk for terrestrial invertebrates that may come into contact with wicks contained within traps or the carrier material; however, these effects would be incidental and localized.

Risk to aquatic vertebrates and invertebrates is also expected to be negligible based on the use pattern for naled in the exotic fruit fly program. There is a wide margin of safety for acute risk to fish based on a highly conservative assumption that a trap containing naled would be deposited into water and would not degrade (figure 5-1). There is some overlap between the range of acute aquatic invertebrate toxicity values and potential naled residues. Species that could be impacted in this exposure scenario include cladocerans; however, the risk is actually much less when considering the rapid degradation of naled in the environment and the unlikely probability that a trap would be deposited into surface water.

Figure 5-1. Acute aquatic risk characterization for naled.



Estimates of chronic risk to fish and aquatic invertebrates were not included in the figure because only one value for each group could be located in the literature. The lowest NOEC for fish was reported as 6 µg/L which is above the range of residues, suggesting low risk to fish from chronic exposure to naled. The 21-day life cycle NOEC for *D. magna* was reported as 0.098 µg/L, suggesting chronic risk to naled exposure in both a wetland and pond scenario. The risk characterization in this exercise did not assume any degradation of naled, which in aquatic systems is very rapid. Therefore, the actual chronic risk would be low to aquatic invertebrates. Risks to aquatic plants that may serve as food and habitat for aquatic vertebrates and invertebrates is negligible based on the available toxicity data for algae, diatoms, and aquatic macrophytes.

6.0 UNCERTAINTIES AND CUMULATIVE IMPACTS

The uncertainties associated with this risk evaluation arise primarily from lack of information about the effects of naled, its formulations, metabolites, and potential mixtures to non-target organisms that can occur in the environment. These uncertainties are not unique to this assessment but are consistent with uncertainties in HHERAs with any environmental stressor. In addition, there is uncertainty in where an exotic fruit fly detection may occur in a specific state, and the rest of the United States, and the extent of naled use in a given infestation because its use is based on site-specific factors.

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

Naled is used for mosquito control and a variety of agricultural uses including food and non-food crops. Its annual use in the United States is approximately 1,000,000 lbs of a.i. (approximately 70% used in mosquito control and approximately 30% in agriculture) (USEPA, 2002). The estimated agricultural use of naled on oranges is 2,000 lbs a.i. annually with less than 1% of the crop being treated (USEPA, 2008d). APHIS fruit fly use of naled is much less and infrequent compared to normal agriculture use (approximately 0.698 g a.i. of naled is in each trap and 1,000 traps per square mile resulting in 1.5 lb a.i. used per square mile).

Cumulative impacts may occur from naled use in relation to other chemicals used in the program that have a similar or different mode of action, and can result in synergism, potentiation, additive, or antagonistic effects. The potential for co-exposure to other pesticides (e.g., DDVP) within the program with the same toxic action may also occur. The other pesticides used in the fruit fly eradication program include spinosad, lambda-cyhalothrin, DDVP, diazinon, and malathion. Spinosad causes over-activation of the central nervous system of insects via the nicotinic ACh receptors. Lambda-cyhalothrin disrupts normal nerve function by inhibiting the closing of the voltage-gated membrane sodium channels of nerve cells. DDVP, diazinon, and malathion are also OP pesticides with the same toxic mode of action as naled. However, cumulative impacts from the proposed use of naled are expected to be incrementally minor due to the proposed use pattern of naled, DDVP, and malathion, and the historical low frequency of positive exotic fruit fly detections. In addition, not all of these products would be used in the program to treat an exotic fruit fly outbreak.

USEPA (2006) completed an assessment of cumulative risks from exposures to all of the OPs as required by the Food Quality Protection Act of 1996. USEPA concluded that the 31 OP pesticides (including naled, DDVP, malathion, diazinon, and others) pending the results of the OP cumulative assessment are indeed eligible for reregistration, and the pesticide tolerances covered by the Interim Reregistration Eligibility Decisions and Tolerance Reassessment and Risk Management Decisions of the OPs meet the safety standard under Section 408(b)(2) of the United States Federal Food, Drug, and Cosmetic Act.

7.0 REFERENCES

Active Mineral International, LLC. 2017. Safety Data Sheet for Material Name: Min-U-Gel ®, Florigel®, Acti-Sorb®, SDS ID: AM-006_NA, issue date: February 14, 2017, Revision 3.1, 9 pp.

AMVAC. 2013. DIBROM® 8 Emulsive Naled Insecticide label, USEPA Reg. No. 5481-479. 12 pp.

AMVAC. 2014. DIBROM® CONCENTRATE Insecticide label, USEPA Reg. No. 5481-480. 7 pp.

AMVAC. 2015a. Safety Data Sheet for DIBROM® 8 Emulsive, 843 Version #: 01, Issue date: 04-03-2015. 12 pp.

AMVAC. 2015b. Safety Data Sheet for DIBROM® Concentrate, 1486 Version #: 01.1, Issue date: 08-14-2015. 11 pp.

Bargar, T. 2012. The relationship between total cholinesterase activity and mortality in four butterfly species. Environ. Toxicol. Chem. 31(9):2124-2129.

California Department of Pesticide Regulation (CDPR). 2007. Registration for Special Local Need for Distribution and Use only within California, Dibrom Concentrate, SLN # CA-860005. 3 pp.

CDPR. 2013. FIFRA 24(c) Special Local Need Label (SLN) for use in traps to control of fruit flies (Tephritidae spp.) DIBROM® 8 Emulsive, SLN # CA-090011. 4 pp.

ChemLDplus. 2016. 4-(p-Acetoxyphenyl)-2-butanone. NIH Toxnet, available at: https://chem.nlm.nih.gov/chemidplus/rn/3572-06-3, last accessed May 16, 2017.

European Commission. 2001. Opinion of the Scientific Committee on Food on Methyleugenol (4-Allyl-1,2-dimethoxybenzene), Scientific Committee on Food, SCF/CS/FLAV/FLAVOUR/4 ADD1 FINAL 26 September 2001, 10 pp.

Florida Department of Agriculture and Consumer Services. 2016. Letter on a specific exemption for the use of naled (Dibrom Concentrate Insecticide), EPA Registration Number 5481-480, in a baiting program for the control and eradication of Tephritid fruit flies in the state of Florida (File Symbol 16-FL-07), dated June 28, 2016.

Hoang, T.C., Pryor, R.L., Rand, G.M., and R. A. Frakes. 2011. Use of butterflies as nontarget insect species and the acute toxicity and hazard of mosquito control insecticides. Env. Tox. Chem. 30(4): 997-1005.

Hudson, R.H., Tucker, R.K., and M.A. Haegele. 1984. Handbook of toxicity of pesticides to wildlife. 2nd Ed. 90 pp.

Maki, A.W., Stewart, K.W., and J.K.G. Silvey. 1973. The effects of Dibrom on respiratory activity of the stonefly, *Hydroperla crosbyi*, hellgrammite, *Corydalus cornutus* and the Golden shiner, *Notemigonus crysoleucas*. Trans. Am. Fish. Soc. 102(4):806-815.

Muncy, R.J., and A.D. Oliver Jr. 1963. Toxicity of ten insecticides to the red crawfish, *Procambarus clarkii*. Trans. Am. Fish. Soc. 92(4):428-431.

National Institute of Health (NIH). 2016a. Naled: CASRN:300-76-5. Toxnet, Hazardous Substance Data Bank, available at: https://toxnet.nlm.nih.gov/cgi-bin/sis/search2/f?./temp/~93gBBk:1, last accessed April 16, 2018.

NIH. 2016b. Dichlorvos: Dichlorvos: CASRN:62-73-7. Toxnet, Hazardous Substance Data Bank, available at: https://toxnet.nlm.nih.gov/cgi-bin/sis/search2/f?./temp/~93gBBk:2, last accessed April 16, 2018.

National Research Council (NRC). 1983. Risk assessment in the Federal government: managing the process. National Academy Press, Washington, DC.

National Toxicology Program (NTP). 2014. Report on Carcinogens, Thirteenth Edition**.** Research Triangle Park, NC: U.S. Department of Health and Human Services, Public Health Service. http://ntp.niehs.nih.gov/pubhealth/roc/roc13/

Sanders, H.O. 1970. Pesticides toxicities to tadpoles of the western chorus frog, *Pseudacris triseriata* and Fowler's toad, *Bufo woodhousii fowleri*. Copeia 2:246-251.

Torchio, P.F. 1973. Relative toxicity of insecticides to the honey bee, alkali bee and alfalfa leafcutting bee (Hymenoptera: Apidae, Halictidae, Megachilidae). J. Kansas Entomol. Soc. 46(4):446-453.

Torchio, P.F. 1983. The effects of field applications of naled and trichlorfon on the alfalfa leafcutting bee, *Megachile rotundata*. J. Kansas Entomol. Soc. 56(1):62-68.

United States Department of Agriculture Animal and Plant Health Inspection Service (USDA APHIS). 2013. Plant health/Pests and Diseases/Programs/Insects/Fruit Flies, Available at: http://www.aphis.usda.gov/wps/portal/aphis/ourfocus/importexport?1dmy&urile=wcm:path:/aphis_content_library/sa_our_focus/sa_plant_health/sa_domestic_pests_and_diseases/sa_pests_and_diseases/sa_insects/sa_fruit_flies/ct_fruit_flies_home, last accessed Nov. 7, 2014.

United States Environmental Protection Agency (USEPA). 1997. Memorandum. RE: EFED's Registration Chapter C for Naled, 41 pp.

USEPA. 1999. Memorandum. Naled. Revised HED risk assessment for RED. USEPA OPP Health Effects Division, October 1999.

USEPA. 2001. Memorandum, Naled: Report of the Hazard Identification Assessment Review Committee. USEPA OPP Health Effects Division, Report dated May 29, 2001.

USEPA. 2002. Interim Reregistration Eligibility Decision for Naled, Prevention, Pesticides and Toxic Substances (7508C), EPA 738-R-02-008 January 2002

USEPA. 2006. Finalization of Interim Reregistration Eligibility Decisions (IREDs) and Interim Tolerance Reassessment and Risk Management Decisions (TREDs) for the Organophosphate Pesticides, and Completion of the Tolerance Reassessment and Reregistration Eligibility Process for the Organophosphate Pesticides, dated July 31, 2006.

USEPA. 2008a. Memorandum, Registration review – preliminary problem formulation for the ecological risk assessment of naled, dated Dec. 10, 2008, 27 pp., available at: https://www.regulations.gov/document?D=EPA-HQ-OPP-2009-0053-0003, last accessed March 2, 2016.

USEPA. 2008b. Risks of Naled Use to Federally Threatened California Red Legged Frog (*Rana aurora draytonii*), Pesticide Effects Determination, Environmental Fate and Effects Division Office of Pesticide Programs, February 19, 2008.

USEPA. 2008c. Memorandum, updated review of naled incident reports, dated October 30, 2008, available at http://www.regulations.gov/#!documentDetail;D=EPA-HQ-OPP-2009-0053-0006, last accessed March 8, 2016.

USEPA. 2008d. Naled (034401) Screening Level Usage Analysis (SLUA), dated August 27, 2008.

USEPA. 2009. Memorandum, Naled. Human Health Assessment Scoping Document in Support of Registration Review, dated January 29, 2009, 13 pp, available at: https://www.regulations.gov/document?D=EPA-HQ-OPP-2009-0053-0005, last accessed April 11, 2017.

USEPA. 2010. USEPA Data Call-In Response for Naled, ID# GDCI-034401-969, dated 28-September-2010.

USEPA. 2012a. U.S. Environmental Protection Agency Endocrine Disruptor Screening Program Universe of Chemicals, available at http://www.epa.gov/sites/production/files/2015-07/documents/edsp_chemical_universe_list_11_12.pdf, last accessed March 8, 2016.

USEPA. 2012b. U.S. Environmental Protection Agency Endocrine Disruptor Screening Program Universe of Chemicals and General Validation Principles, available at http://www.epa.gov/sites/production/files/2015-08/documents/edsp_chemical_universe_and_general_validations_white_paper_11_12.pdf, last accessed March 8, 2016.

USEPA. 2012c. Memorandum – Naled, Immunotoxicity study in Rats, dated July 19, 2012, 12 pp. available at: https://www.regulations.gov/document?D=EPA-HQ-OPP-2009-0053-0050, last accessed May 30, 2017.

USEPA. 2014. Memorandum – Human Health Evaluation Manual, Supplemental Guidance: Update of Standard Default Exposure Factors, OSWER Directive 9200.1-120, 7 pp.

USEPA. 2015a. Annual Cancer Report 2015, Chemicals Evaluated for Carcinogenic Potential Office of Pesticide Programs, U.S. Environmental Protection Agency.

USEPA. 2015b. Endocrine disruption, Endocrine Disruptor Screening Program (EDSP) Estrogen Receptor Bioactivity, available at: http://www.epa.gov/endocrine-disruption/endocrine-disruptor-screening-program-edsp-estrogen-receptor-bioactivity, last accessed March 8, 2016.

USEPA. 2016a. Risk assessment – human health risk assessment (http://www.epa.gov/risk/human-health-risk-assessment), last updated on October 3, 2016, last accessed April 11, 2017.

USEPA. 2016b. Occupational Pesticide Handler Unit Exposure Surrogate Reference Table, November 2016, available at: https://www.epa.gov/sites/production/files/2016-11/documents/handler-exposure-table-2016.pdf, last accessed April 11, 2017.

Zhong, H., Hribar, L.J., Daniels, J.C., Feken, M.A., Brock, C., and M.D. Trager. 2010. Aerial ultra-low volume application of naled: impact on nontarget imperiled butterfly larvae (*Cyclargus thomasi bethunebakeri*) and efficacy against adult mosquitoes (*Aedes taeniorhynchus*). Environ. Entomol. 39(6):1961-1972.