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Draft Risk Evaluation Summaries for Attractants used in the Fruit Fly Eradication Program

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Agency Contact:

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

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EXECUTIVE SUMMARY

APHIS uses various attractants and preservatives in its exotic fruit fly eradication program. The selection of a particular attractant is based on the species being targeted for monitoring and eradication. The following attractants and preservatives are currently used in the program:

- ammonium acetate
- ammonium bicarbonate
- borax (preservative)
- cuelure
- methyl eugenol
- propylene glycol (preservative)
- protein hydrolysate
- putrescine
- torula yeast pellets
- trimedlure
- trimethylamine

Borax and propylene glycol are used as a preservative in traps while the other compounds serve as attractants for fruit flies either as a pheromone or food attractant. These attractants are used in traps for detection and eradication efforts related to various species of exotic fruit flies. All of the products are used exclusively in traps, with the exception of protein hydrolysate, which may also be mixed with an insecticide and applied by ground or air to vegetation.

The toxicity profile for the various chemicals used in traps along with their proposed use pattern demonstrates low risk to human health and non-target organisms. Liquid lures are applied to wicks and other materials, such as plugs that are contained within various trap types that can be used in the Program. The use of traps minimizes exposure of all the attractants to the human population, including the public, as well as the environment. The attractants may attract some non-target terrestrial invertebrates. These impacts are expected to be localized and specific to insects that may be attracted to a specific food attractant or an insect pheromone, or attracted to insects that are caught in the trap.

Ammonium Acetate

APHIS uses ammonium acetate as an attractant in traps to attract male and female *Rhagoletis* spp. (Pelz-Stelinski et al., 2006). Ammonium acetate is an inert ingredient approved by the U.S. Environmental Protection Agency (USEPA) for non-food use.

Ammonium acetate is an ammonium salt of acetic acid. Ammonium acetate has a similar chemical structure, environmental fate, and aquatic and mammalian toxicity profile to acetic acid. USEPA uses toxicity data on acetic acid because there is limited data available for ammonium acetate (USEPA, 2015a). Ammonium acetate has an acute intraperitoneal injection median lethal dose (LD_{50}) of 632 milligram/kilogram (mg/kg) in rats and an acute intravenous injection LD_{50} of 98 mg/kg in mice. Acetic acid has low acute oral toxicity (LD_{50} >3,310 mg/kg in rats and LD_{50} >4,960 mg/kg in mice), moderate acute dermal toxicity (rat LD_{50} >1,060 mg/kg), and very low acute inhalation toxicity (rat median lethal concentration (LC_{50}) >11.4 mg/Liter (L)). Acetic acid caused dermal irritation in mice at greater than 100 mg/kg. Acetic acid also caused skin corrosiveness and acute eye irritation in rabbits (USEPA, 2015a).

Two 28-day oral gavage toxicity studies using ammonium acetate and Wistar or Sprague Dawley rats found different overall toxicities. With Wistar rats, the study reported a low observed adverse effect level (LOAEL) of 100 mg/kg/day based on histopathological lesions in the brain, liver and kidney. The study observed signs of neurotoxicity, such as mild chromatolysis of nuclear material, moderate gliosis, occasional neuronal vacuolation and edema in the cortex of the brain, moderate neuronal degeneration and pyknosis in the nuclei of pyramidal neurons in the hippocampal region, and moderate pyknosis and necrosis in Purkinje neurons in the cerebellum. In contrast, a second study using ammonium acetate and Sprague Dawley rats with the same dose and duration reported a no observed adverse effect level (NOAEL) of 100 mg/kg/day. This study did not find ammonium acetate-related clinical signs or effects on body weight, clinical chemistry, absolute or relative organ weights, gross necropsy, or in the histopathology of the brain, liver or kidneys. There was no indication of systemic toxicity, neurotoxicity, neuropathological or histological lesions in this study (USEPA, 2015a).

A 90-day oral toxicity study in rats administered acetic acid in drinking water reported a NOAEL of 390 mg/kg/day with a non-adverse effect of reduction in weight gain, which was likely due to reduced appetite and food consumption. An inhalation toxicity study with acetic acid in rats and mice observed decreased activity, behavioral changes, and reduced work capacity at 10 mg/kg/day (LOAEL) with a NOAEL of 7 mg/kg/day. The developmental toxicity studies with acetic acid in rats, mice, or rabbits observed no maternal and developmental toxicity at up to 1,600 mg/kg/day and no fetal susceptibility. There do not appear to be any reproductive toxicity studies using acetic acid (USEPA, 2015a).

There is little information on the immunotoxicity of ammonium acetate. An inhalation study exposing rats to acetic acid observed increased spleen weight at 23–31 parts per million (ppm) due to red blood cell destruction instead of an immunotoxic response (USEPA, 2015a). USEPA concluded there is no concern for potential immunotoxicity because residential exposure to the registered use of ammonium acetate via inhalation (shorter duration to diluted acetic acid) is expected to be much lower than the American Conference of Governmental Industrial Hygenists' threshold limit value of 10 ppm for occupational inhalation exposure (8 hours continuously to more concentrated acetic acid).

Based on a search of available literature, there is no information regarding whether ammonium acetate or acetic acid are endocrine disruptors. Ammonium acetate or acetic acid have not been screened under the USEPA Endocrine Disruptor Screening Program (USEPA, 2017a).

There was no evidence of carcinogenicity in an oral toxicity study in rats and there was a negative response for mutagenicity (USEPA, 2015a). The study dosed animals with acetic acid via gavage for 8 months and observed hyperplasia in the esophagus and forestomach, but no tumors. Acetic acid was not mutagenic in an Ames test or clastogenic in a cytogenetic assay.

USEPA (2015a) concluded that there are no toxicological endpoints of concern from exposure to ammonium acetate for the U.S. population, including infants and children based on the lack of toxicity observed in the available studies and its chemical properties. Risk to workers and the general public from APHIS' use of ammonium acetate as an attractant in traps is expected to be negligible based on the lack of toxicity at relevant doses and low probability of exposure.

Ammonium acetate does not persist in the environment. It has a vapor pressure of 0.00014 mm Hg at 20^{o}C and can volatilize to the atmosphere. Ammonium acetate dissociates into the ammonium cation and acetate anion in aqueous solution (USEPA, 2015a). Acetic acid degrades in the presence of microbes with an aerobic half-life of about a day (USEPA, 2015b).

Ammonium acetate is not expected to be toxic to aquatic organisms, mammals, and birds based on a literature review and USEPA's evaluation of acetic acid (USEPA, 2015b, 2014; 2017b). Acetic acid is a naturally occurring substance found in plants, animals, and humans. Acetic acid is practically non-toxic to terrestrial mammals in acute studies, and is not expected to pose acute or chronic risk to birds and mammals. Acetic acid has low risk to insects based on available data with an LD_{50} > 50 micrograms (µg)/honey bee in an acute contact toxicity study. In another study, acute exposure of 26,225 mg active ingredient of acetic acid per hive reported no mortality to honey bees or varroa mites inhabiting the hive. Acetic acid is practically non-toxic to fish with acute LC_{50} values ranging from 303–515 mg/L for the rainbow trout (*Oncorhynchus mykiss*) and slightly toxic to the freshwater cladoceran (*Daphnia magna*) with a 48-hour median effective concentration (EC_{50}) of 65 mg/L (USEPA, 2017b, 2014). Toxicity to non-target aquatic plants is also low with median inhibition concentrations (IC_{50}) ranging from 844.3 to 1,582.9 mg/L. USEPA (2015b) concluded that the potential risk of acetic acid to aquatic organisms is expected to be minimal based on current labeled uses and the buffering capacity of water that

would counteract any pH-related impacts of acetic acid entering water bodies. The use of ammonium acetate in the fruit fly program also eliminates the potential for exposure to aquatic organisms because it is used in traps and would not be subject to offsite runoff or drift. Exposure and risk may occur for some terrestrial non-target invertebrates, especially in the Biolure trap where ammonium acetate is part of a 3-component lure that may attract some non-target invertebrates (LeBlanc et al., 2010).

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Ammonium bicarbonate

APHIS uses ammonium bicarbonate in traps as a source of ammonia to attract fruit flies. Ammonium bicarbonate is a natural chemical that slowly degrades in the environment to ammonia, carbon dioxide, and water. Ammonium bicarbonate is a Food and Drug Administration (FDA) approved food additive, and a USEPA approved inert pesticide ingredient (USEPA, 2004).

There are no identified toxic endpoints for ammonium bicarbonate (USEPA, 2004). The reported acute oral LD_{50} of 1,576 mg/kg in rats indicates low mammalian toxicity (PubChem, 2017). The reported acute intravenous LD_{50} was 245 mg/kg in the mouse. Ingestion at large doses may cause adverse health effects with possible nausea and vomiting. Inhalation may cause respiratory irritation, and contact with eye and skin may cause irritation (Toxnet, 2012). The potential exposure to ammonium bicarbonate in traps is expected to be minimal to workers following the program safety requirements and proper personal protection equipment, and not expected in the general public (APHIS, 2015). As a result, adverse health risks to humans from the program use of ammonium bicarbonate are expected to be negligible.

Ecological effects data is limited for ammonium bicarbonate (USEPA, 2017). The reported no observed effect level (NOEL) and lowest observed effect level (LOEL) of ammonium bicarbonate is 100 mg/kg and 300 mg/kg soil for nematodes, respectively (Oka and Pivonia, 2002). Ammonium bicarbonate has estimated LC_{50} values of 37.1 mg/L (4 days) and 15.6 mg/L (7 days), and a no observed effect concentration (NOEC) of 8.4 mg/L, and a lowest observed effect concentration (LOEC) of 22.8 mg/L in exposures using the leopard frog (Sparling and Harvey, 2006). The NOEC was reported to be 1.08 millimolar (mM) in rainbow trout. USEPA did not identify any toxicological endpoints during registration evaluation of ammonium bicarbonate as an active ingredient for the olive fruit fly (*Bactrocera oleae*) (USEPA, 2004). There were no adverse effects reported from uses of ammonium bicarbonate as a pesticide inert ingredient (USEPA, 2004). The exposure and risks of ammonium bicarbonate to non-target organisms from APHIS use is minimal except for targeted fruit fly species and some non-target invertebrates that may be attracted to traps.

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Borax (Sodium Tetraborate Decahydrate)

APHIS uses borax as a preservative in Torula yeast pellets or with Nu-Lure® insect bait in exotic fruit fly traps (APHIS, 2004, 2015). Boric acid and its sodium salts are registered with USEPA for use as an active ingredient in insecticides, acaricides, herbicides, algaecides, fungicides, and wood and material preservatives used in agricultural, residential, and commercial settings (USEPA, 2015a). Additionally, boric acid and its sodium salts are inert ingredients in pesticide products as well as ingredients in non-pesticide consumer products.

Borax has low acute mammalian toxicity via oral, inhalation, and dermal routes of exposure (Toxicity Category III for oral (LD_{50} = 4,550/4,980 mg/kg in males/females rats, and LD_{50} > 974 mg/kg in dogs) and dermal (LD_{50} >2,000 mg/kg in rabbits), and Toxicity Category IV for inhalation (LD_{50} >2.03 mg/L in rats)). It is corrosive to the eye (Toxicity Category I), but is not irritating to the skin (Toxicity Category IV) (USEPA, 2006, 2015a). Acute oral studies in rats reported a NOAEL of 350 mg/kg, and a LOAEL of >439 mg/kg boron equivalents based on clinical signs of depression, shallow/rapid respiration, diarrhea, red crust on eyes, and mortality (USEPA, 2015a). An in vivo dermal absorption study in humans indicates that very low dermal absorption (<1%) of boric acid/borate salts occurs across intact skin. Subchronic and chronic oral toxicity studies in the mouse, rat, and dog indicate that the testis is the major target organ of boric acid/boric salts with effects such as seminiferous tubule degeneration, reduction in sperm count, atrophy, and reduced testicular weights. Other toxic effects of boric acid/boric salts in animal studies include hematological changes and decreased body weight as well as clinical signs of neurotoxicity (such as hunched posture, abnormal gait, and rapid respiration) at high doses. Epidemiological studies of workers exposed to high levels of borax dust indicate respiratory, sensory, and eye irritation. Human case reports of accidental poisonings from boric acid or borate salt compounds identified clinical signs of central nervous system toxicity including convulsions, headaches, tremors, and restlessness (USEPA, 2015a). Developmental effects include skeletal variation and malformations, and enlarged lateral ventricles in the brain. There was increased pre-natal susceptibility of skeletal and visceral variations and malformations and decreased fetal body weights observed in the rat, mouse, and rabbit. A 28-day mouse immunotoxicity study reported a decreased sheep red blood cell anti-antibody-forming plaque cells response. Borax is considered “not likely to be carcinogenic to humans”. There was no evidence of mutagenic or clastogenic potential based on available genotoxicity studies. There was no indication of boron exposure-related cancers in humans based on epidemiological data (USEPA, 2015a).

Based on the program use of borax in traps, the potential exposure to borax is expected to be minimal to workers and the general public. As a result, adverse health risks to humans from program use of borax as a preservative in traps will be negligible.

Borax is slightly toxic to freshwater invertebrates (an acute 48-hour EC_{50} of 22.8 mg test substance (t.s.)/L in water flea) and practically non-toxic to fish (96-hour LC_{50} levels of 134 mg t.s./L in rainbow trout and 280 mg t.s./L in bluegill sunfish) (USEPA, 2015b). Boric acid is

practically nontoxic to slightly toxic to freshwater and marine invertebrates (*e.g.*, an acute 48-hour EC_{50} of 260 mg acid equivalents (a.e.)/L (45.5 mg boron (B)/L in daphnids, and a 96-hour LC_{50} of 80.1 mg a.e./L (14.0 mg B/L) in whiteleg shrimp) (USEPA, 2015b). Available data shows boric acid to be practically non-toxic (a.e. basis) to slightly toxic (B basis) to fish (*e.g.*, acute 96-hour LC_{50} values of 404 mg a.e./L (70.6 mg B/L) in fathead minnows and 555 mg a.e./L (97 mg B/L) in red sea bream) (USEPA, 2015b). The chronic studies of boric acid in freshwater invertebrate and fish reported NOAEC of 8.9 mg a.e./L (1.6 mg B/L) in daphnids and 42 mg a.e./L (7.4 mg B/L) in fathead minnows. Toxicity studies using boric acid and aquatic non-vascular and vascular plants report an IC_{50} of 81.3 mg a.e./L (14.2 mg B/L) and a NOAEC of 9.2 mg a.e./L (1.6 mg B/L) in freshwater blue-green algae, and an IC_{50} of 163 mg a.e/L (28.5 mg B/L) and a NOAEC of 60 mg a.e./L (11 mg B/L) in duckweed. Borax has low acute mammalian toxicity based on studies in rats and dogs previously discussed in the human health section (USEPA, 2015a). Boric acid and sodium borate salts have moderate toxicity to mammals based on an acute oral LD_{50} of 450 mg a.e./kg-body weight (bw) (79 mg B/kg) in rats (USEPA, 2015b). A chronic toxicity study in mice reported a NOAEL of 150 mg a.e./kg-diet (26 mg B/kg).

Boric acid and sodium borate salts have low toxicity to birds (an acute oral LD_{50} of >1,625 mg a.e./kg-bw (>284 mg B/kg) in bobwhite quail (*Colinus virginianus*), an acute dietary LC_{50} of 11,000 mg a.e./kg-diet (>1,920 mg B/kg), and a NOAEC and a LOAEC of 1,870 mg a.e./kg-diet (327 mg B/kg) and 4,570 mg a.e./kg-diet (799 mg B/kg), respectively in the canary, and a sub-acute dietary LC_{50} of >5,620 mg a.e./kg-diet (>982 mg B/kg) in both bobwhite quail and mallards (*Anas platyrhynchos*)). A chronic bird toxicity study of boric acid reported a NOAEC of 249 mg a.e./kg-diet (43.6 mg B/kg) in the mallard.

Boric acid is practically nontoxic to pollinators such as the honey bee based on a traditional acute contact test of boric acid (LD_{50} of 363 µg a.e./bee, 63 µg B/bee) (USEPA, 2015b). An acute dietary study in dipterans reported a 48-hour LC_{50} of 11,800 mg boric acid/kg-diet for 10-day old males. Dietary exposure of a stingless bee to 0.75 µg boric acid/bee/day for 10 days reported significant decrease in survival (100% mortality by day 10 and 50% mortality of about 7 days), and behavioral changes including wing flapping and accelerated movement (USDA FS, 2016). USEPA's reviews (2015b) of the Ecological Incident Information System, Incident Data System, and the Avian Monitoring Information System for ecological incidents involving boric acid and associated salts identified an incident of a desert tortoise killed by ingestion of borax and two plant damage incidents. USEPA's further search on the aggregate database (1990 to 2015) identified 802 animal and 4 plant incidents. The plant incidents are all associated with a swimming pool algaecide. Among the animal incidents, more than half (469 cases) were caused by Terro® Ant Killer (unspecified) and Terro® Ant Killer II liquid ant bait products, and three cases were caused by a borax product (USEPA, 2015a).

APHIS' use of borax in traps eliminates exposure to aquatic organisms as well as most non-target terrestrial wildlife. Exposure to borax for some terrestrial non-target invertebrates may occur and result in effects to those species that are attracted to the traps.

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Cuelure (4-[p-Acetoxyphenyl]-2-butanone)

Cuelure is structurally related to the sex pheromone produced by female melon flies and is used by APHIS as an attractant in traps to attract male flies. Mammalian laboratory studies (Beroza et al., 1975) show that cue-lure has low acute toxicity with an oral LD_{50} of 3,038 mg/kg (rat), and a dermal LD_{50} of >2,025 mg/kg (rabbit). No adverse effects at concentrations up to 2,800 mg/L in air in an inhalation toxicity study using rats suggests low toxicity from inhalation exposure. USEPA (2005) evaluation during registration indicated that cuelure did not show oral, dermal, or inhalation toxicity, or eye or skin irritation at high doses. The potential exposure to cuelure in traps is expected to be minimal to workers and not expected in the general public. As a result, adverse health risks to humans from the program use of cuelure in traps are expected to be negligible.

Ecological effects data is limited for cuelure; however, available aquatic effects data show moderate to slight toxicity to fish (USEPA, 2017; PubChem, 2017). Beroza et al. (1975) reported 96-hour LC_{50} values of approximately 15 and 16 ppm for the bluegill (*Lepomis macrochirus*) and rainbow trout, respectively. Other reported 96-hour LC_{50} values include 10 and 32 ppm in rainbow trout, and 26.5 and 30 ppm in bluegill (PubChem, 2017). The reported water flea (*Cladocera*) 48-hour EC_{50} values of 28.5 ppm and 39 ppm indicate low toxicity to freshwater invertebrates.

Available terrestrial non-target effects data show that cuelure has low toxicity to mammals, birds, and non-target insects. The reported rat oral LD_{50} of 3,038 mg/kg, and a rabbit dermal LD_{50} value of greater than 2,025 mg/kg, as discussed previously, indicate low toxicity to mammals. A reported acute oral LD_{50} of 2,250 mg/kg in bobwhite quail and dietary LC_{50} value of >5,620 ppm in bobwhite quail and mallard (PubChem, 2017) indicate cuelure is practically nontoxic to birds. Cuelure is practically non-toxic to non-target pollinators such as the honey bee based on the acute contact LD_{50} of >100 µg/bee. The use of cuelure in traps eliminates exposure to aquatic organisms as well as non-target terrestrial wildlife. Exposure and risk may occur for some terrestrial invertebrates that are attracted to cuelure. Non-target insects that are attracted to cuelure bait stations and are killed as a result of a sticky trap or insecticide may also include those that are attracted to dead or decaying animal matter (Uchida et al., 2003).

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Methyl Eugenol

APHIS uses methyl eugenol as a male lure in fruit fly traps. Methyl eugenol is a volatile compound naturally occurring in plants such as nutmeg, pimento, lemongrass, tarragon, basil, star anise, and fennel (European Commission, 2001). In the atmosphere, methyl eugenol is degraded by reaction with photochemically-produced hydroxyl radicals. The half-life for this reaction in air is estimated to be 5 hours (Toxnet, 2017). Based upon an estimated Koc (soil organic carbon-water partitioning coefficient) of 140, methyl eugenol released to soil is expected to have high mobility, and methyl eugenol released to water is expected to adsorb moderately to suspended solids and sediment. Based upon an estimated Henry's Law constant of 5.6×10^{-6} atm-cu m/mole, methyl eugenol in the moist soil surface and on the water surface is expected to volatilize. Dissipation half-lives of 6 and 16 hours (at 32 and 22 ^{o}C, respectively) in soil and 6 and 34 hours (at 32 and 22 ^{o}C, respectively) in water have been reported. Methyl eugenol in water is not expected to undergo hydrolysis in the environment due to the lack of hydrolysable functional groups (Toxnet, 2017). Modelling predicted half-lives of methyl eugenol are 8 days in soil and water, and 32 days in sediment. These predicted half-lives suggest that methyl eugenol is expected to reside mainly in the environmental compartment to which it is released (Environment Canada, 2010).

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 FDA classifies methyl eugenol as a "Generally Recognized as Safe (GRAS)" compound suggesting a low hazard to human health.

Methyl eugenol has low acute toxicity (Toxicity Category III) in testing animals for oral (an oral LD_{50} of greater than 1,179 mg/kg), and dermal (a dermal LD_{50} of greater than 2.02 mg/kg) exposure routes, and very low toxicity (Toxicity Category IV) for the inhalation exposure route (an inhalation LC_{50} of greater than 4.8 mg/L without deaths or adverse signs) (USEPA, 2016). Methyl eugenol caused initial eye and skin irritations in primary eye and dermal irritation studies, but cleared out within 24 and 72 hours, respectively (Toxicity Category IV). Methyl eugenol is not a skin sensitizer. Subchronic toxicity studies of methyl eugenol showed increased liver weights in both male and female rats. A methyl eugenol prenatal toxicity study reported a reduction in the average fetal body weight per litter, an increased incidence of unossified sternebra; and increased liver weight in the maternal animals. Methyl eugenol induced a significant increase in testis size in a reproductive study. Chronic toxicology studies in rats and mice reported that relatively high-bolus doses of methyl eugenol administered orally caused hepatic neoplasms (USEPA, 2016).

National Toxicology Program's review (2005) classified methyl eugenol as "reasonably anticipated to be a human carcinogen". The 2-year study in rats showed increased incidence of liver neoplasms and neuroendocrine tumors of the glandular stomach in both male and female

rats, and increased incidence of kidney neoplasm, malignant mesothelioma, mammary gland fibroadenoma, fibroma of subcutaneous tissue, and combined fibroma or fibrosarcoma in male rats. Methyl eugenol caused unscheduled DNA synthesis and methyl eugenol metabolites formed DNA adducts based on the results of mutagenicity studies (USEPA, 2016).

USEPA's human incident search of the Office of Pesticide Program's (OPP) Incident Data System (April 7, 2006 to December 2, 2015) did not identify any individual reports of major incidents involving humans associated with the use of methyl eugenol in insect traps. A search of OPP's Environmental Incident Information System (1970s to January 11, 2016) did not revealed any incidents associated with methyl eugenol (USEPA, 2016).

Methyl eugenol has moderate acute toxicity to freshwater fish with 96-hour LC_{50} values ranging from 6.0 mg/L (rainbow trout) and 8.1 mg/L (bluegill sunfish). USEPA waived aquatic invertebrate, avian acute oral and dietary, terrestrial plant seedling emergence and vegetative vigor, and toxicity studies because exposure is not expected to occur from the methyl eugenol use pattern as a ready-to-use retrievable insect trap.

Methyl eugenol use in traps may attract non-target insects including scavenger flies (Uchida et al., 2006). The same effect was shown for non-target attraction to methyl eugenol traps with an accumulation of dead Oriental fruit flies (Uchida et al., 2007). An accumulation of dead flies inside the methyl eugenol traps can have a synergistic effect of non-target attraction (Uchida et al., 2007; Leblanc et al., 2010). Methyl eugenol lures may attract a small number of non-target flower-associated insects including pollinators and aphid predators, and plant feeding Miridae and Sciaridae when used over large areas (Leblanc et al., 2009). However, there was a relatively small number of insect pollinators (including honeybees) in methyl eugenol traps (0.03 to 0.15 per trap per day), which suggests that this attraction is likely to occur over a short distance. Avoiding the application of methyl eugenol traps to trees during the flowering stage can minimize exposure to pollinators (USEPA, 2016; Leblanc et al., 2009).

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Propylene Glycol

APHIS uses propylene glycol (a 10 percent solution diluted in water) as a preservative for lures or food baits in Multilure® traps (APHIS, 2015). Propylene glycol is a synthetic liquid. It absorbs water and is used to make polyester compounds and as a base for deicing solutions (antifreeze). Propylene glycol is widely used in the chemical, food, and pharmaceutical industries. The FDA has classified propylene glycol as a food additive that is GRAS, and is a solvent for food colors and flavors (21CFR184.1666). Propylene glycol is a bactericide and fungicide registered with USEPA as an air sanitizer and a hard surface disinfectant, as well as an insecticide (such as for fleas and mites) (USEPA, 2007a). Propylene glycol is also an inert ingredient formulated into end-use agricultural and antimicrobial pesticide products.

Propylene glycol has high volatility with a vapor pressure of 0.129 mm Hg at 25 ^{o}C. Propylene glycol in the atmosphere degrades rapidly through photochemical oxidation by reacting with hydroxyl radicals (estimated half-life of 32 hours) (USEPA, 2007b). Propylene glycol in soil rapidly degrades to CO_2 in 4 to 9 days under aerobic and anaerobic conditions. Propylene glycol has a low soil organic carbon-water partition coefficient (Koc = 8) and would be expected to be highly mobile in soil. Propylene glycol is highly miscible with water and can be transported to aqueous media (ATSDR, 2008; USEPA, 2007a). Propylene glycol is not likely to bioaccumulate in aquatic organisms due to its low octanol/water partition coefficient (log Kow of -0.92). The potential for propylene glycol to partition from surface water to air is low based on its low air/water partition coefficient (Henry's Law Constant of 1.31×10^{-10} atm-cu m/mole at 25 ^{o}C). Propylene glycol has low potential for aquatic hydrolysis, oxidation, volatilization, bioconcentration, and absorptivity to soil (USEPA, 2007b). There is a low potential for propylene glycol to be transported to surface or ground water from APHIS program use in traps.

Propylene glycol has low mammalian toxicity (ATSDR, 2008, USEPA, 2007a). The acute oral LD_{50} values range from 8,000 mg/kg to 46,000 mg/kg in rats, 24,800 mg/kg in mice, and 18,350 to 19,600 mg/kg in rabbits and the guinea pig (USEPA, 2007a). Propylene glycol is not an acute irritant to eye and skin, and is not a skin sensitizer (USEPA, 2007a). It does not normally irritate the skin although contact dermatitis may occur after a wide variety of topical preparations. Inhaling propylene glycol mist may result in irritation for some individuals (ATSDR, 2008).

A subchronic (15-week) oral toxicity study in rats reported a NOAEL of 2,500 mg/kg/day (USEPA, 2007a). Another subchronic (140 days) toxicity study of propylene glycol administered to rats via drinking water reported clinical signs (such as central nervous system depression and minor liver abnormalities) at a dose of 13,200 mg/kg/day. There were clinical signs of toxicity (such as loss of balance, marked depression, and analgesia) reported in mice, guinea pigs, and rabbits at extremely high doses (ranging from 18,400-24,900 mg/kg/day following single oral dose exposures of propylene glycol). A subchronic (90-day) inhalation study in rats reported no changes in respiratory rates, minute volumes, or tidal volumes except for a significant increase in the number of goblet cells in the nasal passages at vapors of 1.0 or 2.2 mg/L. Propylene glycol is not a reproductive or developmental toxicant in mice, rats, hamsters, or rabbits, and there is

negligible concern for reproductive or developmental toxicity in humans (NTP, 2004). There is no evidence of propylene glycol being carcinogenic or mutagenic to humans (USEPA, 2007a; ATSDR, 2008). During the USEPA reregistration review, no toxicological endpoints of concern for oral, dermal, or inhalation exposure to propylene glycol were identified, based on available toxicity data (USEPA, 2006). There is no evidence of dermal toxicity and no adverse effects in repeated dose inhalation toxicity studies up to and exceeding the limit dose of 1 mg/L (USEPA, 2007b). USEPA's human incident review did not identify any incidents reported from propylene glycol as an individual chemical exposure (USEPA, 2007a).

Propylene glycol has very low acute toxicity to terrestrial and aquatic animals (USEPA, 2007c). Propylene glycol is practically non-toxic to birds (LD_{50} > 2,000 mg/kg, NOAEL of 2,000 mg/kg), and mammals (LD_{50} > 5,000 mg/kg and NOAEC > 2,500 mg/kg/day). Propylene glycol is practically non-toxic to freshwater fish (LC_{50} values ranging from 710 to 62,000 ppm), freshwater invertebrates (EC_{50} > 110 ppm, NOEC of 110 mg/kg, and LC_{50} ranges from 1,020 mg/kg to 18,340 mg/kg), and estuarine and marine organisms (LC_{50} > 10,000 ppm). Propylene glycol used in MultiLure® traps baited with BioLure has a synergistic effect resulting in increased captures of *Anastrepha* spp. fruit flies (Leblanc et al., 2010). BioLure is a synthetic food attractant consisting of ammonium acetate, trimethylamine hydrochloride, and putrescine.

Adverse health risks to humans from potential exposure to propylene glycol associated with the program use are not expected because of its low toxicity and diluted concentration and adherence to label and program safety requirements. Exposure to non-target animals is unlikely to occur based on the program use of low quantities in traps.

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Protein Hydrolysate

APHIS uses protein hydrolysate as a food attractant in fruit fly traps. Protein hydrolysate is an extract of yeasts or grains acting as a broad-spectrum food attractant for male and female fruit flies (APHIS, 2004). Yeast extract hydrolysate from *Saccharomyces cerevisiae* is registered with USEPA (2004) as a biopesticide for use on all food crops, as well as on turf and ornamental plants. The active ingredient of the yeast extract hydrolysate primarily consists of oxidized amino acids. It also includes nutrients such as vitamins and minerals. There were no toxic effects observed when testing the end product in laboratory mammals. The FDA considers the active ingredient yeast extract hydrolysate as a GRAS product for food use. Yeast extract hydrolysate has a long history of safe use in food and agriculture.

Nu-Lure® is a commercial formulation of hydrolyzed proteins used by the program that acts as a broad-spectrum food attractant for male and female fruit flies (APHIS, 2004). Nu-Lure® Insect Bait (Miller Chemical & Fertilizer Cooperation, 2017) contains 44% of hydrolyzed corn gluten meal and 56% inert ingredients. FDA considers corn gluten meal as a GRAS (21CFR 184.1321). The safety data sheet for the product (Miller Chemical & Fertilizer, LLC., 2016) shows it is not a hazardous substance or mixture according to 29 CFR 1910.1200. However, Nu-Lure® Insect Bait may cause acute oral, dermal, inhalation, and eye irritation. The potential for human exposure from the program use of Nu-Lure® in traps is low by adhering to specified label safety precautions such as avoiding contact with skin or clothing, and wearing suggested personal protective equipment. Adverse health risks to humans are not expected because of the low toxicity of protein hydrolysate and the low potential for exposure.

No ecological toxicity data appears to be available for protein hydrolysate or the Nu-Lure® formulation. The known components of Nu-Lure® suggest low toxicity to non-target organisms and that it would be the least toxic component of a mixture with an insecticide when it is used in aerial or ground broadcast treatments or in traps.

Foliar treatments on fruit fly hosts using protein hydrolysate with an insecticide increase the potential for human exposure and effects to human health and the environment from this attractant. The foliar treatments use a large droplet size (6–8 mm) that reduces the potential for off-site transport. Protein hydrolysate has low toxicity to mammals and would be a low risk to non-target organisms when compared to the insecticides that are mixed with the bait.

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Putrescine (1,4-diaminobutane)

APHIS uses putrescine as a food attractant in fruit fly traps. Putrescine is one of the compounds used in patches or cones of a 3-component (3C) lure (ammonium acetate, trimethylamine, and putrescine) or a 2-component (2C) lure (ammonium acetate and putrescine) as a food-based synthetic attractant for fruit flies. Putrescine is an effective attractant for female and male *Ceratitis capitata* (LeBlanc et al., 2010). For the patches, these compounds are formulated separately and sealed. Each patch has a circular membrane that controls the rate of release of the compound into the air. This lure is also available in a unipack formulation that includes all of the components in a single patch. Additionally, the lure is available in a cone formulation. The cone contained in a polyseal foil bag allows easy positioning within the multilure® trap. A plastic foot on one end of the cone keeps the bait from sticking to the bottom of the trap. The only approved 3C lure formulation is the 3C patch or 3C cone and the only approved 2C lure formulation is the 2C patch or 2C cone (APHIS, 2015).

Putrescine is a polyamine produced by the breakdown of amino acids in living and dead organisms and widely distributed in the human body. Putrescine may act as a growth factor for cell division and apparently has a specific role in skin physiology and neuroprotection. Polyamines play a role in spermatogenesis, skin physiology, promotion of tumorigenesis and organ hypertrophy as well as neuronal protection (NCBI, 2017). Putrescine is considered an indirect additive used in food contact substances by the FDA (2017). Through injection of 1,4-diaminobutane dihydrochloride 97%, the subcutaneous and intravenous LD_{50} values in rats and mice were 1,625 mg/kg and 760 mg/kg and 1,880 mg/kg and 510 mg/kg, respectively. The intraperitoneal LD_{50} in mice was 1,400 mg/kg. Putrescine is a skin, eye, and respiratory irritant. It caused adverse effects such as decreased body weight at high doses in rats (Toxnet, 2011).

Adverse health risks to humans from potential exposure to putrescine associated with the program use are not expected because the compound is formulated in a sealed patch with a controlled release rate into the air.

Ecological effects data is limited for putrescine (USEPA, 2017); however, available terrestrial vertebrate non-target effects data indicates low toxicity to mammals based on a reported oral LD_{50} value of 1,600 mg/kg in deer mouse (Schafer and Bowles, 1985). The use of putrescine in traps eliminates exposure to aquatic organisms as well as most non-target terrestrial wildlife. Exposure and risk may occur for some terrestrial non-target invertebrates that are attracted to putrescine. A study showed that the use of putrescine in the 3C lure attracted large numbers of saprophagous flies (dominated by Drosophilidae in Hawaii) (Leblanc et al., 2010). Based on the study results, the researchers suggested two strategies to reduce potential impacts to rare or endangered species in Hawaii: 1) avoid using lures in native Hawaiian forest, and 2) use a 300 m buffer between endemic forests and the placement of a trap. Aquatic toxicity data does not appear to be available for putrescine; however, the proposed formulation and use pattern would eliminate significant exposure and risk to aquatic organisms.

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Torula Yeast Pellets

APHIS uses Torula yeast pellets as a food attractant in fruit fly traps. Torula yeast pellets are a commercial formulation of yeast protein that acts as a food attractant for male and female fruit flies (APHIS, 2004). It is composed of 45% torula yeast and 55% dry borax decahydrate in pellet form (5 grams each). The pellets are dissolved in water at the ratio of one pellet per every 100 ml of capture fluid (3 pellets/300 ml per trap) to produce the attractant solution placed in McPhail traps (APHIS, 2015).

Yeast is naturally occurring in the environment. It breaks down naturally, and is not expected to accumulate. Yeast is commonly found as an ingredient in many foods. Dried torula yeast is a food additive permitted for addition to food for human consumption (FDA, 2017). USEPA (2009) evaluated yeast used as an attractant during a biopesticide registration review. Based on its safe use in food and its non-toxic mode of action, USEPA waived the guideline toxicity requirement, stating products containing yeast can be used without causing unreasonable adverse effects to humans or the environment (USEPA, 2009). The potential for exposure to torula yeast in traps is expected to be minimal due to workers adherence to label and program safety requirements and not expected for the general public. As a result, adverse health risks to humans from the program use of torula yeast in pellets placed in traps are negligible. No ecological toxicity data appears to be available; however, yeast is expected to have low risk to non-target fish and wildlife due to the low probability of exposure and lack of toxicity in other organisms.

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Trimedlure (4-(or 5) chloro-2-methylcyclohexanecarboxlic acid, 1,1-dimethyl ester)

APHIS uses trimedlure in traps to attract the Mediterranean fruit fly, and many related species belonging to the *Ceratitis* genus (APHIS, 2004). Trimedlure is a synthetic arthropod pheromone registered with USEPA as a biopesticide (USEPA, 2016). Synthetic pheromones modify behavior of the target pest species at concentrations close to those found in nature, and dissipate rapidly (OECD, 2002). Trimedlure is impregnated into a polymeric matrix dispenser that is placed in a trap and slowly dissipates in approximately 6 to 8 weeks (USEPA, 2016).

Trimedlure has low acute mammalian toxicity via oral, dermal, and inhalation routes of exposure (Toxicity Category III for oral (LD_{50} = 4,556 mg/kg in rats) and dermal (LD_{50} >2025 mg/kg in rats), Toxicity Category IV for inhalation (LD_{50} >2.9 mg/L in rats)). It is not irritating to the skin or eyes (Toxicity Category IV) (USEPA, 2001). The safety assessment of other structurally similar pheromone products using two subchronic toxicity studies (90-day oral and developmental) as bridging data indicated that there were no significant health effects from subchronic exposure to this group of compounds (OECD, 2002). USEPA waived the requirements for subchronic studies (90-day oral, dermal, inhalation, mutagenicity, and developmental toxicity studies) for trimedlure because of its low acute toxicity, and lack of significant health effects from subchronic exposure of other structurally similar pheromones (USEPA, 2016). The OPP's Incident Data System from June 21, 2001 (the year of the first trimedlure product registration) through December 2, 2015, did not identify any human health incidents associated with trimedlure (USEPA, 2016).

Program workers are the most likely population with potential for dermal and inhalation exposures to trimedlure during application and handling of dispensers containing trimedlure. The potential exposure for handlers and applicators is anticipated to be minimal because both traps and dispensers are commercially available as ready to use, and the program uses them outdoors, which significantly limits the potential for applicator dermal and inhalation exposure. The potential for adverse health risks is anticipated to be minimal based on the low mammalian toxicity and low potential for exposure.

Exposure to the general public from the use of trimedlure is very low. Risks to the general public are negligible because of low mammalian toxicity, the low rate of product use in a trap, and the low potential for exposure. Incidental exposure and risk to young children is not be expected to be significant due to the low mammalian toxicity and that the trimedlure is contained within enclosed dispensers within traps that are placed out of reach of children.

Ecological effects data are limited for trimedlure; however, available aquatic effects data show moderate toxicity to fish. Beroza et al. (1975) reported 96-hour LC_{50} values of approximately 9.6 and 12.1 ppm for the rainbow trout and bluegill, respectively. Available terrestrial vertebrate non-target effects data are limited to the rat and rabbit with a reported rat oral LD_{50} value of 4,556 mg/kg, and a rabbit dermal LD_{50} value of greater than 2,025 mg/kg. Both values suggest

low toxicity to mammals. USEPA's evaluation during registration review (2016) indicates that pheromones are highly toxic to aquatic invertebrates and moderately toxic to fish, but practically non-toxic to birds (low toxicity to bobwhite quail, with an acute oral LD_{50} of > 2,000 mg/kg of body weight and dietary LC_{50} of > 5,000 mg/kg). APHIS use of trimedlure in traps eliminates exposure to aquatic organisms as well as most non-target terrestrial wildlife. Exposure and risk may occur for some terrestrial invertebrates that are attracted to trimedlure or to the dead insects in the traps (Uchida et al., 2006).

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Trimethylamine (Methanamine, N,N-dimethyl)

APHIS uses trimethylamine as a food attractant in traps. Trimethylamine is one of the compounds used in patches or cones of a 3C lure along with ammonium acetate and putrescine as food-based synthetic attractants. These compounds are formulated separately in sealed patches. Each patch has a circular membrane that controls the rate of release of the compound into the air. The lure is also available in a unipack formulation that includes all of the components in a single patch. For a cone formulation, the cone contained in a polyseal foil bag allows easy positioning within the multilure® trap (APHIS, 2015).

Trimethylamine is a naturally occurring substance that forms from the decomposition of plants and animals. In the environment, trimethylamine is present at low concentrations. Trimethylamine is a plant nutrient and will not accumulate in the environment. It has fly-attracting properties because the odor suggests a food source or medium suitable for depositing fly eggs (USEPA, 2009). Due to its proposed use and natural occurrence in the environment, USEPA waived acute, subchronic, and other mammalian toxicity test requirements during registration evaluation.

Trimethylamine has low acute oral toxicity (LD_{50} of 500 mg/kg in rats) (USEPA, 2009, NIOSH, 2017) and very low acute inhalation toxicity (LC_{50} of 19 gm/m^3 in mouse) (NIOSH, 2017). However, it is a sensory irritant if inhaled at 61 ppm (USEPA, 2009). Trimethylamine is corrosive to skin and eyes (USEPA, 2009). A concentrated solution of trimethylamine applied to human skin caused severe burning and hyperemia, and accidental human eye contact with trimethylamine can cause corneal epithelial sloughing (NIH, 2009). Trimethylamine in food is generally regarded as non-toxic (FDA, 2013).

Adverse health risks to the human population, including the public, from exposure to trimethylamine are not expected because the compound is formulated in a sealed patch or a cone contained within a trap and has a slow controlled release rate (USEPA, 2009).

Limited ecological effects data is available for trimethylamine. USEPA waived a majority of the studies required for biopesticide registration because exposure is not anticipated due to the use of trimethylamine in packets or cones inside traps (USEPA, 2009). This use of trimethylamine eliminates exposure to terrestrial and aquatic non-target organisms suggesting negligible risk. Published data show aquatic toxicity to be low for most test species. Tonogai et al. (1982) reported a median threshold limit of 1,000 mg/L in 24- and 48-hour trimethylamine exposures using the Japanese medaka (*Oryzias latipes*). A review of other amines demonstrate low toxicity to fish and aquatic invertebrates with effect values typically exceeding 100 mg/L (Poste et al., 2014). Terrestrial invertebrates including honeybees and other beneficial insects are not expected to be attracted to or adversely affected by the use of trimethylamine in a fly trap because insects classified as “filth flies” are the primary insect taxa attracted to traps when trimethylamine is

used as a mixture for attracting flies (USEPA, 2009). LeBlanc et al. (2010) demonstrated that trimethylamine by itself was not attractive to non-target terrestrial invertebrates in traps set in a variety of habitats in Hawaii. Trimethylamine used in combination with ammonium acetate and putrescine was more effective in attracting fruit flies and other non-target terrestrial invertebrates than trimethylamine alone.

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