Overview of Malathion
Risk Assessment
September 2005

Introduction

This document summarizes EPA's human health and ecological risk findings and conclusions for the organophosphate pesticide malathion. The purpose of this summary is to assist the reader by identifying the key features and findings of these risk assessments, and to better understand the conclusions reached in the assessments.

The revised human health risk assessments "*Malathion: Updated Revised Human Health Risk Assessment for the Reregistration Eligibility Decision Document*" dated September 13, 2005 and ecological risk assessment "*EFED Environmental Risk Assessment for the Malathion Reregistration Eligibility Document*" May 01, 2000 are available on the Internet (http://www.epa.gov/pesticides/op/malathion.htm) and the EPA, Office of Pesticide Programs (OPP) public docket.

Use Profile

- **Technical Registrants** - Cheminova Agro A/S

- **Type of Pesticide -** Nonsystemic, wide spectrum organophosphate insecticide.

- **Use Sites** - Malathion is a broad-spectrum organophosphorous (OP) insecticide, widely used in agriculture and regional pest eradication programs. Some of these uses are not being supported for reregistration and will not be considered in this risk assessment. The following use sites and crops are being supported and were included in this risk assessment.

- **Food and Feed Crops -** Alfalfa; apple; apricot; asparagus; avocado; barley; bean (succulent and dry); beets (garden, table, and sugar); birdsfoot trefoil; blackberry; blueberry; boysenberry; broccoli; broccoli raab; Brussels sprout; cabbage (including Chinese); carrot; cauliflower; celery; chayote; cherry; chestnut; clover; collards; corn (field; sweet; and pop); cotton; cucumber; currant; dandelion; date; dewberry; eggplant; endive; escarole; potato; fig; flax; garlic; gooseberry; grape; grapefruit; guava; hay grass; hops; horseradish; kale; kohlrabi; kumquat; leek; lemon; lespedeza; lettuce (head and leaf); lime; loganberry; lupine; macadamia

nut; mango; melon; mint; mushroom; mustard greens; nectarines; oats; okra; onion; orange; papaya; parsley; parsnip; passion fruit; pea; peach; pear; pecan; pepper; pineapple; pumpkin; quince; radish; raspberry; rice; rutabaga; rye; salsify; shallot; sorghum; spinach; spring wheat; squash; strawberry; sweet potato; Swiss chard; tangelo; tangerine; tomato (including tomatillo); turnip; vetch; walnut; watercress; watermelon; wheat (spring, and winter); wild rice; and yam; indoor stored commodity treatment and empty storage facilities for barley, corn, oats, rye, and wheat.

- **Other Uses -** Homeowner outdoor uses: ornamental flowering plants, ornamental lawns, ornamental turf, vegetable gardens and fruit trees; golf course uses; ornamental flowers, shrubs, and trees; Christmas tree plantations; slash pine; ornamental nursery stock; woody plants; building perimeters (domestic dwellings as well as commercial structures); uncultivated nonagricultural areas; outdoor garbage dumps; intermittently flooded areas; irrigation systems; sewage systems; pastures; and rangeland.

- **Regional Pest Eradication Programs** - Boll Weevil eradication (USDA sponsored program), Medfly control (USDA), and mosquito control (public health).

- **Pharmaceutical Malathion** - There is a non-FIFRA pharmaceutical use of malathion as a pediculicide for the treatment of head lice and their ova, which is regulated by the Food and Drug Administration (FDA). A separate assessment of this use is available in the docket.

- **Types/Formulations Registered** - Malathion is formulated as an emulsifiable concentrate (EC), dust (D), wettable powder (WP), ready-to-use (RTU) liquid, and as a pressurized liquid (PrL). The EC and RTU formulations may contain up to 82% and 96.5% active ingredient (ai), respectively. Several of the 96.5% ai RTU liquids are intended for ultra-low-volume (ULV) application with the use of aerial or ground equipment. Malathion is typically applied as multiple foliar treatments as needed to control various pest species.

- **Application Equipment** - Aircraft (fixed wing, and rotary), duster, fogger, ground boom, irrigation, shaker can, shovel, sprayer, and spreader .

- **Target Pests** - Ants, aphids, apple mealybug, armyworm, bagworm, beetle, borer, casebearer, blackheaded fireworm, blueberry maggot, cadelle, caterpillars, cattle lice, cherry fruitworm, cockroaches, corn earworm, corn rootworms, cotton fleahopper, cotton leaf perforator, cotton leafworm, cranberry fruitworm, crickets, currant cutworm, earwigs, European fruit lecanium, fall cankerworm, fleahoppers, fleas, flies, fruit flies, fungus gnats, garden webworm, grain borer, grape phylloxera, grasshoppers, green cloverworm, greenbug, groundpearls, hornets, imported cabbageworm, imported currantworm, ked, leafhoppers, leafrollers, leafminer, looper, millipedes, mites, mosquitoes (adult, larvae), moths, kermes, mushroom flies, omnivorous leaftier, onion maggot, orange tortrix, orangeworms, pear psylla, pecan phylloxera, pepper maggot, pickleworm, pillbugs, pine needle sheathminer, plant bugs, plum curculio, poultry lice, rose chafer, sawflies, scales, scorpions, silverfish, sorghum midge,

sowbugs, spiders, spittlebugs, springtails, strawberry leafroller, sugarbeet root maggot, tadpole shrimp, thrips, ticks, tingids, tomato fruitworm, vetch bruchid, wasps, weevil, whiteflies, wild rice worm.

- **Typical Usage** - An average annual estimate of total domestic usage of malathion is 16.7 million pounds of malathion as active ingredient (ai). Approximately 12.5 million pounds ai is applied to agricultural crops, of which nearly 90% (11.2 million pounds) is applied to cotton through the USDA Boll Weevil Eradication Program. Another 0.3 million pounds ai is applied as postharvest grain treatment to corn, wheat, and oats. Approximately 0.5 million pounds ai are used for agricultural sites such as around buildings, roads, and ditches. Approximately 3.4 million pounds are applied to non-agriculture sites, such as Medfly quarantine, under Section 18, (emergency exemption), (800,000 pounds), mosquito abatement (472,000 pounds), golf courses, and homeowner outdoor insect control.

  A summary of the use patterns of malathion is presented in Table 1.

Table 1. Summary of Use Patterns for Malathion

Market Segment	Use Sites	Formulation	Application Method	Application Rate (lb/a.i./A) unless noted	Application Timing
USDA Programs	Cotton Boll Weevil Eradication Program	EC (ULV)	Aerial is preferred, but ground is also used around sensitive areas	0.3 to 1.5	First year: 6-8 applications, every 7-10 days Second year: only as pest problem indicates
	Medfly Control (Section 18)	EC (ULV) mixed with protein bait as spray	Aerial Ground (backpack and truck-mounted sprayers)	0.175	Application frequency and intervals between application are based on pest pressures specific to the Section 18 exemption.
General Agriculture	Food/Feed[1,2] * Alfalfa * Cotton * Rice * Sorghum * Wheat	EC (including ULV) WP	Aerial Groundboom Airblast	0.15 to 6.0	Most schedules call for application when pest first appears, with repeat applications as necessary, always observing the pre-harvest intervals (PHIs). See Residue Chemistry Chapter, Table A2 for more details
	*Stored grains[3] *Empty grain storage bins	Dusts	Power Duster	1-10	Apply to cleaned storage bins prior to loading. Apply to grain as it is being transported, or loaded into storage bin.
	Non-Food/Feed[1] * Ornamentals * Roadways * Turf/sod farms * Commercial Forests * Industrial sites	EC	Aerial Groundboom Airblast Sprayer Handgun (turf sprayer) Low Pressure Handwand Backpack Sprayer Hose End Sprayer Power Duster (bins only)	2.6 to 8.7	Most schedules call for application when pest first appears, with repeat applications as necessary.
Public Health	Mosquito Control	EC (ULV)	Aerial Ground (truck-mounted aerosol generators)	0.11 to 0.5	Used as adulticide with applications depending on pest presence
Home/Garden	* Turf * Vegetable Garden * Ornamentals	50% and 57% EC, some dusts	Low Pressure Handwand Backpack Sprayer Hose End Sprayer Shaker Can Fogger	0.000085 to 0.0003 lb/ft^2	For fruit trees: at new spring growth, repeat as necessary every 7-10 days For turf: every 3-4 weeks as necessary For others: as necessary

[1] Representative of major use sites; not a complete listing.
[2] These five crops represent more than 50% of malathion use in the United States and have the highest use-rates proposed by the registrant.
[3] The stored grain commodities on which malathion dust can be used on are as follows: corn, oats, barley, rye, and wheat

Human Health Risk Assessment

Hazard Characterization

EPA has a substantially complete database on malathion sufficient to characterize potential hazard to individuals, including sensitive individuals such as young children. Additional data has been received and reviewed by the Agency since 2000, including a developmental neurotoxicity study and a comparative cholinesterase study. The Agency considered all relevant data when selecting the current endpoints for the measurement and characterization of malathion hazard. Throughout the data, in acute, subchronic, and chronic studies, the primary target of malathion is the nervous system. Cholinesterase (ChE) inhibition was seen in multiple species (rat, mouse, rabbit, and dog) and across compartment (blood, plasma and brain). The Agency has chosen inhibition of cholinesterase in the blood (RBC ChEI) as the primary endpoint for the malathion risk assessment. With the exception of the toxicity endpoint for acute dietary exposure and incidental oral exposure, all endpoints to characterize the hazard of malathion have remained unchanged from the Agency's 2000 risk assessment. All hazard endpoints are summarized below in Table 2.

A comparative ChE study with rats was submitted to the Agency in 2000. These data have been chosen to set the toxicity endpoint for acute dietary and incidental oral exposure. The Agency analyzed these data using the bench mark dose (BMD) model. BMD analysis is a more refined, robust analysis of a data set in comparison to dose response analysis using NOAELs and LOAELs. The BMD analysis of the comparative ChE study provided refined estimates of the differential sensitivity juveniles and adults display when exposed to malathion. Based on these data, the Agency has included in its current assessment of malathion an FQPA Special Safety Factor (10x) to be protective of developing individuals.

Carcinogenicity

The Agency has classified malathion as "suggestive evidence of carcinogenicity but not sufficient to assess human carcinogenic potential." The classification is based on the following evidence: 1) the occurrence of liver tumors in mice and rats only at excessive doses; 2) the presence of a few rare tumors in rats, which cannot be distinguished as either treatment related or due to random occurrence; 3) the evidence for mutagenicity is not supportive of a mutagenic concern in carcinogenicity; and 4) malaoxon, a structurally related chemical, is not carcinogenic in rats. The carcinogenic potential of malathion was also reviewed by the FIFRA Scientific Panel (SAP) on August 17-18, 2000. The Panel report, "A Consultation on the EPA Health Effects Division's Proposed Classification of the Human Carcinogenic Potential of Malathion," dated December 14, 2000, offers an overall equivocal recommendation on the Agency's classification of malathion as "suggestive." The Agency subsequently considered the SAP recommendations and concluded that the cancer classification should remain as "suggestive." The Agency has also reviewed a 2001 publication which showed malaoxon to be negative for carcinogenicity.

FQPA Safety Factor Considerations

Federal Food Drug andCosmetics Act (FFDCA), as amended by FQPA, directs the Agency to use an additional tenfold (10x) special safety factor, to account for potential pre-and post-natal toxicity and completeness of the data with respect to exposure and toxicity to infants and children. FQPA authorizes the Agency to modify the tenfold safety factor only if reliable data demonstrate that the resulting level of exposure would be safe for infants and children. Use of an FQPA factor of 10x for malathion is reasonable given the susceptibility ratio seen between adults and young using the BMD analysis of the comparative ChE assay in rats. It is believed that if the residual toxicological issues were fully characterized, the magnitude of difference from the current conservative assessment would likely be less than 10x. For all the malathion endpoints, the Agency employed traditional intra-species (10x) and inter-species (10x) uncertainty factors.

The proposed endpoints and doses for the malathion risk assessment are based on, or consider, the most sensitive population, i.e., the developing individual. Where an endpoint relevant to children in the U.S. population has been selected using adult animal data, as opposed to pup animal data, the Agency applied the FQPA Special Safety Factor of 10x. The endpoints where the FQPA Special Safety Factor for developing individuals was included are: the chronic dietary end point, the dermal endpoint for children, and the inhalation endpoint for children. These endpoints therefore, have a 1000x safety factor. A 10x factor was applied to the inhalation endpoint for adults because the lowest dose tested in that study resulted in effects on the epithelium. Table 2 summarizes safety factors and uncertainty factors used for the current revised human health risk assessment.

Table 2. Summary of Toxicological Doses and Endpoints for Malathion Human Health Risk Assessment

Exposure Scenario	Dose (mg/kg/day), Uncertainty Factors, and Safety Factors	Population Adjusted Dose (PAD) or Target Margin of Exposure (MOE)	Study and Toxicological Effects
Dietary Risk Assessments			
Acute Dietary (Females 13-49)	There is no increased susceptibility expected to females of child-bearing age. Effects observed in the rat and rabbit developmental studies showed reduced body weight gains with NOAELs of 400 and 25 mg/kg/d, respectively. The aRfD for the general population is lower and thus would be protective of this population group.		
Acute Dietary (General population including infants and children)	NOAEL = 13.6 mg/kg UF = 100x[1] (inter. + intra.) FQPA SF = 1x[2] Acute RfD = 0.14 mg/kg	aPAD = Acute RfD / FQPA SF aPAD =0.14 mg/kg/day	Comparative ChE acute oral study in the rat. $BMDL_{10}$[5] = 0.14 mg/kg/day based on RBC ChEI in male pups
Chronic Dietary (All populations)	NOAEL = 3 mg/kg/day[4] UF= 100x (inter. + intra.) FQPA SF = 10x[3] Chronic RfD = 0.03 mg/kg/day	cPAD = Chronic RfD / FQPA SF cPAD = 0.003 mg/kg/day	NOAEL =3 mg/kg/day based on RBC ChEI in females in chronic/ carcinogenicity oral study in the rat (LOAEL = 35 mg/kg/day)
Non-Dietary Risk Assessments			
Short- (1-30 days) and Intermediate- Term (1 - 6 Months) Incidental Oral	Oral $BMDL_{10}$[5] = 7.1 mg/kg/d UF = 100x (inter. + intra.) FQPA SF = 1x	Residential MOE = 100[6] (Short-term only) Occupational MOE = N/A	Comparative ChE multiple dose oral study in the rat $BMDL_{10}$ = 7.1 mg/kg/d based on RBC ChEI in offspring.
Short- (1-30 days) and Intermediate- Term (1 - 6 Months) Dermal (children)[2]	Dermal NOAEL = 50 mg/kg/day UF = 100x (inter. + intra.) FQPA SF = 10x (susceptibility of young)	Residential MOE = 1000[7] (Short-term only) Occupational MOE = N/A	LOAEL = 300 mg/kg/day based on plasma and RBC ChEI (♂, ♀) and brain ChEI (♀) in 21-day dermal study in rabbits.
Short- (1-30 days) and Intermediate- Term (1 - 6 Months) Dermal (adults)	Dermal NOAEL = 50 mg/kg/day UF = 100x (inter. + intra.)	Residential MOE = 100 (Short-term only) Occupational MOE= 100	LOAEL = 300 mg/kg/day based on plasma and RBC ChEI (♂, ♀) and brain ChEI (♀) in 21-day dermal study in rabbits.
Long-term (>6 mo) Dermal (adults)	Dermal NOAEL = 50 mg/kg/day UF = 100x (inter. + intra.)	Residential MOE = N/A Occupational MOE = 100	LOAEL = 300 mg/kg/day based on plasma and RBC ChEI (♂, ♀) and brain ChEI (♀) in 21-day dermal study in rabbits

Exposure Scenario	Dose (mg/kg/day), Uncertainty Factors, and Safety Factors	Population Adjusted Dose (PAD) or Target Margin of Exposure (MOE)	Study and Toxicological Effects
Short- (1-30 days) and Intermediate-term (1 - 6 Months) Inhalation (all populations)[8]	Inhalation LOAEL= 25.8 mg/kg/day (0.1 mg/L) UF = 100x (inter. + intra.) SF = 10x (LOAEL to NOAEL + severity of effect)	Residential MOE = 1000[9] (Short-term only) Occupational MOE = 1000[8]	LOAEL= 25.8 mg/kg/day (0.1 mg/L) based on histopathology in respiratory epithelium 90-day inhalation study in rats
Short-term (1-30 days) and Intermediate-term (1-6 mo) Inhalation **(children) Aggregate Only**	Inhalation NOAEL= 25.8 mg/kg/day (0.1 mg/L) UF = 100x (inter. + intra.) FQPA SF = 10x (susceptibility of young)	Residential MOE = 1000[7] (Short-term only) Occupational MOE = N/A	LOAEL = 0.45 mg/L (115 mg/kg/day) based on plasma and RBC ChEI 90-day inhalation study in rats
Short-term (1-30 days) and Intermediate-term (1-6 mo) Inhalation **(adults) Aggregate Only**	Inhalation NOAEL= 25.8mg/kg/day (0.1 mg/L) UF = 100x (inter. + intra.)	Residential MOE = 100 (Short-term only) Occupational MOE = 100	LOAEL = 0.45 mg/L (115 mg/kg/day) based on plasma and RBC ChEI 90-day inhalation study in rats
Cancer	**Classification:** Suggestive evidence of carcinogenicity		

UF = uncertainty factor, FQPA SF = Special FQPA safety factor, NOAEL = no observed adverse effect level, LOAEL = lowest observed adverse effect level, PAD = population adjusted dose (a = acute, c = chronic) RfD = reference dose, MOE = margin of exposure, LOC = level of concern, NA = Not Applicable

[1] UF = 100 [10x for interspecies and a 10x for intraspecies variations was used].

[2] FQPA factor of 1 used because susceptibility of the young already accounted for because they were part of the experimental group.

[3] A 10x FQPA Safety Factor was used to account for differences in susceptibility observed in the comparative ChE study.

[4] The combined chronic/onco study in rats low dose level was 100 ppm in the diet for 3 months which was dropped to 50 ppm in the diet for the remainder of the study (21 months). The calculated dose for the 3-month exposure was 8-9 mg/kg/d. The calculated dose from the 21 month exposure was 2-3 mg/kg/d. Assuming that a LOAEL for ChEI effects could be 8 mg/kg/d (effects that prompted a lowering of the dose to 2-3 mg/kg/d), then an appropriate NOAEL would be 3 mg/kg/d.

[5] Benchmark Dose Lower Limit (BMDL), lower 95% confidence limit on the RBC CheI 10% effect level. Doses used in the study were: 0, 5, 50, and 150 mg/kg/d.

[6] MOE = 100 [10x for interspecies extrapolation, 10x for intraspecies variations]. Susceptibility of the young already accounted for because they were part of the experimental group.

[7] MOE = 1000 [10x for interspecies extrapolation, 10x for intraspecies variations, and 10x for known susceptibility of the young based on the comparative ChE study].

[8] Absorption via the inhalation route is assumed to be equivalent to oral absorption.

[9] MOE = 1000 [10x for interspecies extrapolation, 10x for intraspecies variations, and 10x for a LOAEL to NOAEL extrapolation and for the severity of the effect.]

Cumulative Risk Characterization/Assessment

The Food Quality Protection Act of 1996 requires EPA to consider potential human health risks from all pathways of dietary and non-dietary exposures to more than one pesticide acting through a common mechanism of toxicity. The Agency has determined that the organophosphate pesticides share a common mechanism of toxicity: inhibition of acetylcholinesterase through phosphorylation of the active site. Malathion is an organophosphate pesticide and is included in the Agency's cumulative risk assessment for this class of pesticides. The Agency has completed a revised organophosphate (OP) cumulative risk assessment which was released to the public for comment in the Federal Register on June 20, 2002 (67 FR 41993). Information about organophosphate pesticides, the OP cumulative risk assessment, and related documents may be found at: http://www.epa.gov/pesticides/cumulative/.

Malaoxon Toxicity

In the current assessment of malathion, the Agency has also refined its characterization of the potential hazard from, and exposure to malaoxon, the oxygen analog of malathion. Malaoxon is the active cholinesterase inhibiting component of malathion products and therefore is a more potent cholinesterase inhibitor than malathion *per se*. Due to its fate and chemistry, exposure to malaoxon, occurs either through (1) treated drinking water where malathion converts to malaoxon during the chlorination process, or (2) in settings where individuals may come into contact with hard, dry surfaces on which malathion residues have been deposited and allowed to remain there for some time. Due to a lack of data, uncertainties exist with respect to EPA's estimate of potential exposure to malaoxon. The Agency is requesting additional information and data on the potential exposure to malaoxon through the public participation process and possibly through data requirements of the technical registrant.

The toxicity of a metabolite has been characterized in terms of its degree of potency in comparison to the parent compound. The ratio of relative toxicity is referred to as the Toxicity Adjustment Factor (TAF). Ideally, separate TAFs are used for acute and chronic exposures. However, the Agency has only limited toxicity data on malaoxon; currently only two chronic studies on malaoxon are available. Based upon the two available studies, the Agency has calculated a chronic TAF of 77x, and in the absence of data to calculate an acute TAF, the Agency used the chronic TAF for all exposure durations, routes, and scenarios. The Agency has required an acute toxicity study with malaoxon to help address this uncertainty which it expects to receive in late 2005. As with exposure information on malaoxon, the Agency is soliciting additional malaoxon toxicity data through the public participation process.

Dietary Exposure and Risk

Dietary Risk (Food)

Tier 3, probabilistic acute and refined chronic dietary risk assessments were conducted using the Lifeline Model Version 2.0 and Dietary Exposure Evaluation Model (DEEM-FCID J, Version 2.02) using food consumption data from the U.S. Department of Agriculture=s Continuing Surveys of Food Intakes by Individuals (CSFII) from 1994-1996 and 1998. Malathion residue estimates reflect use of monitoring data, processing factors, and percent crop treated (%CT) data and include the oxygen analog metabolite malaoxon. Pesticide residue data were included from USDA-PDP monitoring data from 1999-2003, and FDA & FOODCONTAM data, which analyzed for malathion and malaoxon. The toxicity adjustment factor (TAF) of 77x calculated from oral studies was used to adjust the small number of samples where residues of malaoxon was found on food commodities.

For acute and chronic dietary assessments, risk is expressed as the ratio of expected exposure to the population adjusted dose (PAD). The PAD is the endpoint with the appropriate safety factors applied, and is considered to be the dose which will result in no unreasonable adverse health effects. Estimated dietary (food) risks less than 100% of the PAD, either acute (aPAD) or chronic (cPAD), are not of concern to the Agency.

Table 4 summarizes the acute and chronic dietary risk from malathion and malaoxon from food alone. Acute and chronic dietary risk from malathion residues alone on food is below the Agency's level of concern for all population subgroups at the 99.9th percentile using DEEM-FCID, and Lifeline.

Table 4. Summary of Dietary Exposure and Risk for Malathion to Food Only

Population Subgroup	Acute			Chronic		
	aPAD mg/kg	Exposure mg/kg/day	% aPAD	cPAD mg/kg/day	Exposure mg/kg/day	% cPAD
General U.S. Population	0.15	0.027721	20	0.003	0.000312	8
All Infants < 1 yr.	0.15	0.027917	20	0.003	0.000498	17
Children 1-2 yrs.	0.15	0.063762	46	0.003	0.000817	24
Children 3-5 yrs.	0.15	0.055906	40	0.003	0.000639	21
Children 6-12 yrs.	0.15	0.030488	22	0.003	0.000473	16
Youth 13-19 yrs.	0.15	0.018155	13	0.003	0.000256	8
Adults 20-49 yrs.	0.15	0.021022	15	0.003	0.000300	10
Adults 50+ yrs.	0.15	0.018455	13	0.003	0.000157	5
Females 13-49 yrs.	0.15	0.018455	13	0.003	0.000254	8

Drinking Water Dietary Risk

Exposure to pesticides through drinking water may occur through ground water or surface water contamination. EPA considers both acute (one day) and chronic (lifetime) drinking water risks and uses either modeling or actual monitoring data, if available, to estimate those risks. The Agency conducted an analysis of available monitoring data and a screening-level assessment using Tier II PRZM (Pesticide Root Zone Model) and EXAMS (Exposure Analysis Modeling System) model to estimate the potential concentration of malathion and its degradate malaoxon in surface water sources of drinking water.

Based on fate characteristics, model predictions and actual monitoring studies, the Agency predicts malathion will reach drinking water sources. However, insufficient targeted monitoring studies are available to adequately define acute malathion/malaoxon concentrations in drinking water; thus, surface water concentrations associated with a range of malathion uses were conservatively modeled. Based upon laboratory data and analysis of available drinking water facility monitoring data, EPA believes that any concentrations of malathion entering a drinking water treatment facility are completely converted to malaoxon under the standard chlorination process. Therefore, estimated drinking water concentrations have been adjusted by the TAF of 77x to account for 100% conversion of malathion to malaoxon.

Twenty-six different crop/location scenarios were analyzed in order to represent the wide range of use patterns and locations where malathion is used in the U.S. Based on screening-level modeling results for surface water derived drinking water, use of malathion on Florida citrus (aerial application, at maximum application rate) results in the highest one-in-ten year peak (18.4 ppm) and annual mean (0.201 ppm) concentration. The lowest annual peak concentration (0.46 ppm) and annual mean concentration (0.003 ppm) was modeled from the use of malathion on Oregon apple (airblast application, at typical application rates). These concentrations represent estimated malathion concentrations which are fully converted to malaoxon, and which have been adjusted by the TAF (77x).

EPA does not add potential drinking water exposure from surface water sources with ground water sources, doing so would overestimate potential exposure. Instead, EPA uses the greater of the two concentration estimates (ground water or surface water). Table 5 presents estimated malaoxon concentrations in drinking water from surface water sources.

Table 5. Summary of Estimated Surface Water Concentrations for Malathion and Malaoxon

Exposure Duration	Malaoxon Concentrations	
	Florida Citrus Adjusted for TAF-77X (ppm)	Oregon Apple Adjusted for TAF-77X (ppm)
Acute	**13.0** **16.9** **18.4**	0.36 0.39 0.46
Chronic (non-cancer)	**0.201**	0.003

Non-Dietary Exposure and Risk

Potential non-dietary exposure from malathion may result from the home (outdoor only) and garden uses, including vegetable gardens, home orchards, and ornamentals. Non-dietary exposure may also occur from the wide-area treatments for mosquito control, or during fruit fly applications, or as a result of drift from agricultural uses. There is also the potential for exposure to individuals near cotton fields treated with malathion as part of the USDA sponsored Boll Weevil Eradication Program. The Agency believes that non-dietary exposure to malaoxon may also occur as a result of the mosquito control, fruit fly and/or the Boll Weevil use of malathion; and, that non-dietary exposure to malaoxon would not result from the home and garden uses of malathion. Below the Agency has assessed exposure to the malathion per se, and has assessed the non-dietary exposure and risk from malathion as well as malaoxon.

Residential Exposure and Risk (Malathion per se)

Residential Handler Risk

Malathion is used around the home and garden primarily on roses and other ornamentals, on edible food crops, and also as a perimeter treatement around homes. In assessing exposure from these uses, the Agency considers that only adults, not children, would be involved in mixing, loading and applying of pesticides around residential settings. Further, the use of personal protective equipment (PPE), and engineering controls are not considered acceptable opitons for products sold for use by homeowners.

In these settings, malathion can be applied by garden hose end sprayer, low pressure handwand, by backpack sprayer, and as a fogger unit. Residential handler exposure via the dermal and inhalation routes can occur from handling, mixing, loading, and applying (M/L/A) malathion products. Five residential handler exposure scenarios were identified for malathion which included:1) M/L/A a liquid with a low pressure handwand; 2) M/L/A a wettable powder with a low pressure handwand; (3) L/A a liquid with a hose end sprayer; (4) M/L/A a liquid with a backpack sprayer; and, (5) M/L a liquid for fogger application. Exposure duration for a residential handler is considered short-term (1-30 days), based on label directions, frequency of use, and the relatively short environmental half-life, therefore, no intermediate- or long-term assessment was performed.

- For handlers of malathion at residential settings, combined MOE's (dermal and inhalation) for all handler scenarios do not exceed the Agency's level of concern. Total MOE's range from 100 to > 5,000.

Residential Post Application Risk

The Agency believes that there is potential contact with malathion residues from working in treated home gardens, from the activities of individuals at commercial "pick-your-own"strawberry fields, as well as outdoor activities that may follow use of malathion fogging units. Residential postapplication scenarios likely to result in exposure to malathion residues include: 1) dermal exposure from residues on vegetable/small fruit gardens; 2) dermal exposure from residues while harvesting fruit and nut trees; 3) exposure to residues from "pick-your-own" strawberries, and 4) inhalation exposure from airborne malathion following fogger use at residential, park, and school sites. As discussed in a later section, additional postapplication exposure can occur as a result of off-target spray drift from one of the wide area applications of malathion (Boll Weevil Eradication Program, public health mosquitocide use, or fruit fly (Medfly) treatment).

- Postapplication dermal MOEs for adults range from 106 to 1800, with a target MOE of 100, and adult inhalation MOE's from outdoor fogger treatments are estimated to be 1800 with target of 1000, and therefore, do not exceed the Agency's level of concern.

- The postapplication MOE estimate for children exposed via inhalation from outdoor fogger treatments is estimated to be 90, with a target MOE of 1000, which therefore exceeds the Agency's level of concern.

Residential Co-Exposure Risks from Handling and Post-Application Activities

When it is reasonable to assume that an individual may be exposed to the same compound through different activities on the same day or in the same time period, then the Agency combines the different routes of exposure. Combined MOE's for adults who may be exposed to malathion residues from both residential handling as well as from residential postapplication activities were also calculated. Margins of exposure from these scenarios range from 105 - 263, and therefore do not exceed the Agency's level of concern. A combined postapplication MOE estimate was not conducted for toddlers since the Agency currently estimates that postapplicaiton inhalation exposure alone exceeds the Agency's level of concern.

Wide-Area Treatment Post Application Risk (Malathion per se)

EPA assessed potential exposure and risk from malathion's wide-area treatment uses, which include malathion use as a public health mosquitocide, malathion use in the USDA Boll Weevil Eradication Program, and fruit fly (Medfly) treatment uses. For all three wide-area treatment scenarios, the Agency assessed adult exposure via the dermal and inhalation route, and assessed toddler exposure via the dermal, inhalation and the oral route. Oral exposure may occur when a child places into its mouth either its hand, soil or grass, or an object which may have pesticide residues on the surface, this route of exposure is termed "incidental oral." When

calculating the combined MOE's for toddler exposure from the wide-area uses of malathion, the Agency combined the endpoints with different levels of concern (dermal exposure endpoint, with inhalation endpoint, with the incidental oral endpoint for example), into an aggregated risk index (ARI). An ARI greater than 1 does not exceed the Agency's level of concern. The target MOE for combined adult exposures is 100.

Public Health Mosquito Uses

Potential postapplication exposure to adults and children may occur from ultra low volume (ULV) aerial and ground-based applications of malathion for public health mosquito control used in the vicinity of residential dwellings. Exposure scenarios assessed include: 1) dermal exposure from residues deposited on turf (adult and toddler); 2) incidental oral exposure from residues on turf, and objects (toddler only); 3) incidental oral exposure from accidental ingestion of soil with pesticide residues (toddlers only); and, 4) inhalation exposure (adult and toddler).

- Risk estimates for adults for malathion per se are above the Agency's level of concern. MOE's are estimated to be greater than 9000.

- The postapplication ARI for toddlers from public health application are estimated to be greater than 2.8, and therefore not of concern.

Boll Weevil Eradication Program

The Agency performed an assessment for non-occupational bystander exposure from malathion ULV applications to cotton as part of the Boll Weevil Eradication Program. The Boll Weevil Eradication Program is a special project under the direction of the United States Department of Agriculture aimed at eradicating the boll weevil pest in cotton-growing regions in the U.S. Since the program is sufficiently different from conventional agricultural use, the EPA conducted a separate exposure analysis from this use.

- Combined dermal and inhalation MOE for adults from malathion alone is estimated to be greater than 2000, and therefore not of concern.

- Combined dermal, inhalation, and incidental oral ARI for toddlers from malathion alone was estimated to be greater than 6, and therefore not of concern.

Fruit Fly (Medfly) Control

EPA assessed the potential exposure resulting from direct deposition of malathion ULV residues in residential areas during area-wide treatment for fruit flies. Similar to the exposure scenarios assessed for public health mosquitocide treatment, exposure scenarios from fruit fly application include (1) dermal exposure from residues deposited on turf (adult and toddler); (2) incidental oral exposure from residues on turf, and objects (toddler only); (3) incidental oral exposure from accidental ingestion of soil with pesticide residues (toddler only); and, (4) inhalation exposure (adult and toddler).

- Combined MOE for adult postapplication exposures (dermal and inhalation) following aerial fruit fly application are estimated to be greater than 1000, and therefore are not of concern.

- Combined toddler ARI for postapplication exposures (dermal, inhalation, and incidental oral) estimated to be 0.66, and therefore, represents a potential risk concern. Toddler risk is driven by dermal exposure to residues on turf resulting from inadvertent drift.

***Residential Exposure and Risk (Malaoxon*)**

Under some conditions, malaoxon can be formed as an environmental breakdown product of malathion. Data indicate that while malaoxon presence on foliage is nearly negligible, it can be present in air, soil, sand, and that the formation of malaoxon is greatest on hard, dry surfaces. For these reasons, EPA believes that contact with residues deposited on hard, dry surfaces following aerial application of malathion present the most relevant and worst case scenario for assessing risk from malaoxon exposure. Specifically, EPA has estimated potential exposure to malaoxon on wood decks and playground equipment following aerial applications and has focused on exposure to toddlers who may contact malaoxon residues on these surfaces following one of the wide area uses of malathion.

Malaoxon residues are determined by starting with estimated malathion residues and adjusting these residues by the malathion-to-malaoxon transformation factor (1%, 5%, or 10%), and then adjusting these values by the toxicity adjustment factor of 77x. (Estimates of the potential rate of malaoxon formation ranges from 1% to 10%.) The untransformed malathion is also accounted for in estimating exposure from aerial drift. Combined malathion and malaoxon exposure is expressed as average daily doses (ADD) in mg/kg/day and compared to the appropriate common toxicity endpoint to determine the combined risk.

Malaoxon Residential Risk Characterization

Postapplication risk to toddlers from potential contact with malathion and malaoxon residues on dry, hard play surfaces may occur as a result of off-target drift following one of the wide area applications (public health mosquitocide, boll weevil, and fruit fly treatments). The Agency assumed maximum application rates and employed deposition values derived from the AgDrift model. The Agency used the mean transfer coefficient, and assumed a child may play on a hard, play surface for one hour. EPA calculated MOEs using these assumptions along with a range of transformation rates of 1%, 5%, and 10%; as a result, EPA has developed a range of potential MOE's (Table 6) for toddler exposure to both malathion and malaoxon from contact on hard dry surfaces following wide area applications with malation. Due to the uncertainties around several of the variables necessary to estimate exposure (such as deposition from drift, and the rate of transformation), EPA has requested additional data and information through the public participation process to reduce uncertainties and refine its risk characterization of malaoxon.

Table 6. Malathion + Malaoxon Estimated MOEs for Toddler from Wide Area Uses

Use Pattern	Exposure Route/ LOC	MOE Range[1]	ARI
Public Health	dermal LOC = 100	2,500 - 190,000	2.1 - 160
	hand-to-mouth LOC = 1000	1,300 - 99,000	
Boll Weevil Eradication Program	dermal LOC = 100	530 - 2,500	0.5 - 2.1
	hand-to-mouth LOC = 1000	300 - 1,500	
Fruit Fly Treatment	dermal LOC = 100	1,100 - 5,200	0.9 - 4.5
	hand-to-mouth LOC = 100	590 - 3,000	

1: range captures MOE estimates made with 1%, 5%, and 10% transformation of malathion to malaoxon, and for aerial application and ground application methods as well.

Aggregate Risk

In accordance with the FQPA, EPA must consider and aggregate pesticide exposures and risks from three major sources: food, drinking water, and residential exposures. In an aggregate assessment, exposures from relevant sources are added together and compared to quantitative estimates of hazard (e.g., a NOAEL or PAD), or the risks themselves can be aggregated. When aggregating exposures and risks from various sources, EPA considers both the route and duration of exposure.

Aggregate risk assessments were performed for acute and chronic dietary (food + drinking water) exposures using the Dietary Exposure Evaluation Model (DEEM-FCID **J**, Version 2.02). As discussed below, certain exposure scenarios to malathion and malaoxon from dietary (food and drinking water) sources alone exceed the Agency's level of concern, based on results from some drinking water model scenarios. Because risk from dietary sources alone exceed the Agency's level of concern, the Agency did not aggregate residential exposures with dietary exposure as this would only serve to increase the reported risks.

Acute Aggregate Risk

A Tier 3 (highly refined), acute probabilistic dietary exposure assessment was conducted for all supported food uses and drinking water. Residue estimates used in this assessment include malathion and the oxygen analog, malaoxon. Because malaoxon is considered more toxic than malathion, EPA performed benchmark dose modeling to evaluate relative potency for malathion and malaoxon. As noted earlier, a toxicity adjustment factor (TAF) of 77x has been calculated from oral toxicity studies for hazard characterization of malaoxon.

Estimated concentrations of malathion/malaoxon in surface water sources of drinking water were generated by the PRZM-EXAMS model. The Agency assumed 100% conversion of malathion to malaoxon, and predicted malathion concentrations were adjusted with the TAF (i.e., multiplied by 77). As discussed in the drinking water section, the PRZM-EXAMS distributions used in this dietary assessment represent several scenarios. Aerial application to Florida citrus using the maximum application rate resulted in the highest estimated concentrations of malathion in drinking water sources, and the airblast application of malathion to Oregon apples at the typical application rate resulted in the lowest estimated concentrations of malathion in drinking water sources.

The acute dietary exposure estimates for food and drinking water using the worst-case FL citrus crop scenario for drinking water are at the 99.9th percentile of exposure and exceed the Agency's level of concern, i.e. > 100% aPAD. The acute dietary exposure estimates for food and drinking water using the Oregon apple crop scenario for drinking water at the 99.9th percentile of exposure, do not exceed the Agency's level of concern. Tables 7 and 8 summarize acute dietary risk (food + drinking water) for the highest exposure site, citrus (FL), and the lowest exposure site, apple (OR), respectively.

Table 7. Acute Dietary (Food + Water) Aggregate Exposure and Risk Estimates for Malathion and Malaoxon Using the Florida Citrus Scenario at the 99.9th Percentile of Exposure

Population Subgroup	PAD, mg/kg/day	DEEM-FCID	
		Exposure, mg/kg/day	%aPAD
U.S. Population	0.15	0.217679	155
All infants (< 1 yr)	0.15	0.76401	540
Children 1-2 yrs.	0.15	0.331551	236
Children 3-5 yrs.	0.15	0.299780	214

Table 8. Acute Dietary (Food + Water) Aggregate Exposure and Risk Estimates for Malathion and Malaoxon Using the Oregon Apple Scenario at the 99.9th Percentile of Exposure

Population Subgroup	PAD, mg/kg/day	DEEM-FCID	
		Exposure, mg/kg/day	%aPAD
U.S. Population	0.15	0.030304	22
All infants (< 1 yr)	0.15	0.0606046	43
Children 1-2 yrs.	0.15	0.064102	46
Children 3-5 yrs.	0.15	0.058861	42

As mentioned earlier, a total of 26 different crop/location scenarios were analyzed in order to represent the wide range of application conditions and locations where malathion is used in the U.S. Of the 26 scenarios, several, which were based on maximum application rates, resulted in acute aggregate dietary (food and drinking water) risks that exceeded 100% of the aPAD for one or more population subgroups, and therefore exceed the Agency's level of concern. Among the crop/location scenarios that were modeled, the scenarios that resulted in acute dietary risks >100% of the aPAD for the most sensitive population subgroup (all infants < 1 yr.) include the following:

- citrus (FL) aerial and airblast application, at maximum application rates;
- cotton (MS) aerial and ground boom application at maximum application rates;
- sorghum (TX) aerial and ground boom application at maximum application rates; and,
- cabbage (FL) aerial and ground boom application at maximum application rates.

- All scenarios based on typical use rates were below the Agency's level of concern.

Short-Term Aggregate Risk

Aggregate short-term risk estimates include the contribution of risk from chronic dietary sources (food + drinking water) and short-term residential sources. Exposures to malathion from certain dietary (food and water) sources alone exceed the Agency's level of concern. In addition, certain residential postapplication exposure scenarios also exceed the Agency's level of concern. Therefore, estimating a short-term aggregate risk (combining residential exposures with dietary exposures) would only serve to increase the reported risks, and was not conducted.

Long-Term (Chronic) Aggregate Risk

A refined chronic dietary exposure assessment was also conducted for malathion. EPA assessed the potential aggregate chronic dietary (food and drinking water) risk from two crop scenarios, citrus (FL), and apple (OR) using both DEEM-FCID and Lifeline dietary exposure models. Estimated surface water concentrations were based on data from the highest annual mean from FL citrus aerial maximum application rate, and the lowest annual mean from OR apple airblast at typical application rate. Estimated water concentrations were adjusted with the malaoxon TAF of 77x.

The chronic dietary exposure estimates for food and drinking water using the worst-case FL citrus crop scenario for drinking water exceed the Agency's level of concern for the U.S. population and almost all population subgroups. The aggregate chronic dietary exposure estimates using the apple (OR) scenario is below the Agency's level of concern for the U.S. population and all population subgroups. Tables 9 and 10 summarize aggregate chronic dietary risk (food + water) for the highest exposure site, citrus (FL), and the lowest exposure site, apple (OR), respectively.

Table 9. Chronic Dietary (Food + Water) Aggregate Exposure and Risk Estimates for Malathion and Malaoxon Using the Florida Citrus Crop Water Scenario

Population Subgroup	PAD, mg/kg/day	DEEM-FCID		Lifeline	
		Exposure, mg/kg/day	% cPAD	Exposure, mg/kg/day	%cPAD
U.S. Population	0.003	0.0048	149	0.003119	104
All infants (< 1 yr)	0.003	0.014162	472	0.011554	385
Children 1-2 yrs	0.003	0.007006	234	0.006845	228
Children 3-5 yrs	0.003	0.006433	214	0.005904	197

Table 10. Chronic Dietary (Food + Water) Aggregate Exposure and Risk Estimates for Malathion and Malaoxon Using Oregon Apple Water Scenario

Population Subgroup	PAD, mg/kg/day	DEEM-FCID		Lifeline	
		Exposure, mg/kg/day	% cPAD	Exposure, mg/kg/day	%cPAD
U.S. Population	0.003	0.000312	10	0.000311	10
All infants (< 1 yr)	0.003	0.000498	17	0.000394	13
Children 1-2 yrs.	0.003	0.000817	27	0.000664	22
Children 3-5 yrs	0.003	0.000639	21	0.000627	21

Occupational Risk

Workers can be exposed to a malathion through mixing, loading, or applying the pesticide, and re-entering a treated site. There is also potential occupational exposure to individuals that do flagging for aerial applications. Occupational exposure to malathion can be by the dermal or inhalation route. Worker risk is measured by a margin of exposure (MOE) which determines how close the occupational exposure comes to the No Observed Adverse Effect Level (NOAEL) taken from animal studies. Generally, MOEs which are greater than 100 do not exceed the Agency's level of concern. For workers entering a treated site, restricted entry intervals (REIs) are calculated to determine the minimum length of time required before workers or others are allowed to reenter.

Short-term and intermediate-term exposures have been evaluated for field workers. EPA did not assess long-term exposure to field workers since the nature of malathion use is seasonal. However, malathion use in mushroom houses is a special case, where the indoor, nearly year long treatment and harvesting of multiple crops results in potential long-term exposure.

Estimated occupational risk does not include malaoxon since it is not expected to be present during mixing and loading operations, and since malaoxon is not expected to form on plant foliage, there would be no postapplication exposure.

Use patterns of malathion indicate a number of occupational exposure scenarios, based upon the types of equipment and activities used to make malathion applications. The Agency assessed 19 different scenarios taking into account the range of application equipment and application types registered for malathion use.

Short-Term and Intermediate-Term Occupational Risk

Combined dermal and inhalation exposures to handlers are not of risk concern for most mixer/loader scenarios assuming baseline clothing (long pants, long sleeved shirt, shoes and socks) and gloves. For those scenarios that involve high application rates, large area of treatment, or wettable powder formulations, additional clothing, a respirator, or engineering controls are required in order to not exceed the Agency’s level of concern.

Most applicator scenarios do not exceed the Agency’s level of concern. Exceptions include airblast application of emulsifiable concentrate to apricots, cherries, nectarines, peaches avocados, figs, chestnuts, pecans, walnuts, citrus fruits, ornamentals, and applying sprays for mosquitoes with a non-thermal fogger. For these exceptions, the addition of gloves, additional clothing, or headgear provides effective protection. For all flagger scenarios, for all formulations and crops, the Agency’s level of concern is not exceeded when handlers wear baseline level clothing.

Postapplication Risks

The current REI on malathion labels is 12 hours. To calculate "days after treatment" the Agency primarily relied on transfer coefficient data submitted by the Agricultural Reentry Task Force (ARTF), and maximum application rates used in field trial studies to support reregistration. Most activities reach the target MOE of 100 on day zero. However, several crops with medium to high contact activity and using maximum application rates require REIs from 4 - 6 days. See Tables 11 for a summary of reentry exposure and risk estimates.

Human Incidence Report

Incident data were obtained from the OPP Incident Data System (IDS), California Department of Pesticide Regulation, National Pesticide Information Center (NPTIC), and Poison Control Centers. Symptoms commonly reported from malathion exposure from the above sources cover the spectrum normally associated with OP exposure, and include headache, nausea, dizziness, muscle weakness, drowsiness, difficulty breathing, diarrhea, excess secretions, agitation, confusion, blurred vision, and death from accidental or intentional ingestions (i.e., suicides). Analysis of updated incident reports indicates that residential exposures and poisonings have declined in recent years. Recent data also indicate a reduced rate of malathion poisonings in California (0.27 systemic poisonings per 1,000 applications from 1999-2003 as compared to 0.41 poisonings per 1,000 applications between 1982 and 1989).

There are inherent limitations associated with collecting incident data, including inadequate documentation of exposure and effects, reporting biases and absence of denominator information on the population at risk. However, certain consistent patterns of risk factors can be identified. The large majority of malathion incidents appear to involve minor symptoms which may be a reaction to the odor rather than cholinergic poisoning. Broken bottles and other inadequate packaging accounted for over a quarter of the cases in California from 1982 through 1995. Drift was another common cause of incidents in California. In many of these cases, it appears that symptoms are brought on by the offensive odor of the compound alone (i.e., ChE depression need not be present). More serious poisoning cases involve direct exposure to concentrate, resulting from equipment failure or failure to exercise minimal precautions during maintenance or clean-up of equipment for example.

Pharmaceutical Use of Malathion

In addition to the registered pesticide uses, malathion is also produced for use as a pharmaceutical product under the trade name Ovide® Lotion, 0.5% by Taro Pharmaceuticals USA. Ovide Lotion is registered by the Food and Drug Administration (FDA) for the treatment of *Pediculus humanus capitis* (head lice and their ova) of the scalp hair. Ovide Lotion is marketed in 2 fl. oz. bottles and is only available through a doctor's prescription. Patients are directed by the label to use Ovide lotion topically, by applying it to the scalp hair, leaving it on the patient (uncovered) for 8 – 12 hours, then washing it off. The label indicates that application to children should be done under adult supervision.

Ovide Lotion is regulated by the FDA under the Federal Food Drug and Cosmetic Act, (FFDCA); Section 408 of FFDCA requires EPA to consider potential sources of exposure to a pesticide in addition to the dietary sources expected to result from a pesticide use subject to the tolerance. The statute also requires that in order to set or maintain a pesticide tolerance, EPA must "determine that there is a reasonable certainty of no harm…" Under FFDCA section 505, FDA reviews human drugs for safety and effectiveness and may approve a drug notwithstanding the real possibility that some patients may experience adverse side effects.

EPA does not believe that, for the purposes of section 408 dietary risk assessment, it is compelled to treat a pharmaceutical patient the same as a non-patient, or to assume that combined exposures to pesticide and pharmaceutical residues that lead to a physiological effect constitutes "harm" under the meaning of section 408. To do so would lead to the anomalous result that pharmaceutical exposures alone could be considered "safe" for pharmaceutical users under section 505 of the FFDCA and "unsafe" at the same time for the same users under section 408 (since the desired pharmaceutical exposures often will exceed the pesticide "risk cup" level on their own). EPA believes the appropriate way of harmonizing sections 408 and 505 when determining whether exposures to pesticides are "unsafe" for pharmaceutical users is to examine the impact that the additional non-occupational pesticide exposures will have on pharmaceutical patients who may be exposed to a similar substance (or, in some cases, the same substance) through the use of a human drug. Under this approach, EPA must consider the incremental impact of exposure to malathion pesticide residues on the pharmaceutical patient, and therefore, EPA looked to FDA's authority with respect to the safety of a pharmaceutical patient.

EPA provided FDA with estimates of combined pesticide exposure from the non-occupational sources of malathion. EPA provided FDA with a range of exposure estimates, which indicate that the potential exposure from the combined pesticide uses of malathion are approximately 6 - 200x smaller than the malathion exposure a patient is expected to receive from a typical application of Ovide® Lotion. FDA noted that EPA's anticipated high-end non-occupational exposure to malathion (0.27 mg/kg/day) would fall within the expected upper range of exposure following Ovide Lotion, 0.5%, use alone, and would not present an increased safety risk to the patient.

Ecological Risk Assessment

To estimate potential ecological risk, EPA integrates the results of exposure and ecotoxicity using the quotient method. Risk quotients (RQs) are calculated by dividing acute and chronic exposure estimates by ecotoxicity values for various wildlife species. RQs are then compared to levels of concern (LOCs). Generally, the higher the RQ, the greater the potential risk. Risk characterization provides further information on the likelihood of adverse effect occurring by considering the fate of the chemical in the environment, communities and species potentially at risk, their spatial and temporal distributions, and the nature of the effects observed in studies.

Nontarget Terrestrial Animal Risk

Malathion is not expected to pose a hazard to birds and mammals from acute dietary exposure. Chronic exposure to birds is a concern because although malathion is not persistent in the environment, current labels do not restrict consecutive applications, intervals, or avoidance of nesting birds. Lack of label restrictions may result in repeated exposures, at intervals of less than 7 days allowing the buildup of malathion residues over time. Sublethal effects to birds may include reduced nesting behavior, disorientation, and loss of motor coordination leading to reduced ability to cope with other stress factors in the environment. Small mammals may also be sublethally affected at highest application rates

- For avian dietary risk, acute RQs range from 0.001-0.72; chronic RQs rang from 0.01-18.1.
- For small mammals, acute RQs range from 0.10-3.65; chronic RQs range from 0.005-3.0.

Nontarget Aquatic Animal Risk

Malathion is toxic to aquatic organisms. Risk quotients above the Agency's level of concern for nontarget aquatic organisms result from low application rates. Due to its low persistence in water, single applications of malathion are not expected to lead to chronic exposure conditions, however, repeat applications within a one week period may lead to chronic exposure conditions. Concentrations in water can occur as a result of malathion's high potential to drift. Runoff in urban areas has also resulted in relatively high aquatic malathion concentrations. Fish kills attributed to malathion have been (1) in small streams or ponds where slow flow rates permit concentrations to exceed toxic levels for fish or (2) where heavy rainfall events to large watershed areas allowed high concentration pulse loads to impact small aquatic habitat areas, or (3) associated with malathion use in urban areas.

- For aquatic invertebrates, acute RQs range from 8.2-226, and chronic RQs range from 33-931.

- For fish, acute RQs range from 0.3-7.4, and chronic RQs for fish range from 0.04-1.0.

Nontarget Insect Risk

As an insecticide, malathion is expected to impact non-target insects along with the intended target insect pest. Malathion is considered highly toxic to bees at rates routinely used in agricultural settings. Honeybee studies have indicated that foliar residues of malathion are highly toxic 48 hours after application. The use of malathion in wide area applications, such as a public health mosquitocide or for fruit fly applications in urban and rural sites, is expected to impact numerous species other than the intended target insect pests.

Nontarget Plant Risk

Generally, the Agency only requires terrestrial and aquatic plant testing for herbicides. Malathion is not expected to pose a serious hazard to terrestrial plants or aquatic algae as the mode of action (effects to the nervous system) would not apply to plants. The Agency has received no reports of adverse reactions of crops or plants to malathion itself, though label advisories for forest use do caution against application to certain species of trees.

Environmental Incidence Report

The greatest numbers of detailed reports of fish kill incidents involved heavily monitored programs such as USDA's Boll Weevil Eradication Program and the Mediterranean fruit fly eradication efforts. Other incidents appeared linked to uses near aquatic habitats where direct drift may have occurred, such as mosquito control.

- In many of the incidents, use rates and residue levels following the incidents are not clear and kills are investigated days after the event probably occurred.

- In two incidents, sewage discharge was treated with malathion to control flies and then released directly into tributaries.

- In all cases where residue levels are provided, they are within the limits expected to prove toxic to sensitive fish species (>4 ppb).

- Invertebrates are likely to have been more severely effected in fish kill incidents, because fish are less sensitive to malathion than a majority of the invertebrate species tested in laboratories to date.

- In most of the fish kill incidents there appears to have been no effort to investigate the other components of the ecological community in the adversely affected sites.

Summary of Proposed Changes to Use Patterns

The following uses are not being supported for reregistration by the primary data provider, Cheminova. Therefore, these uses were not considered in this risk assessment:

All pet uses for all formulations;
All livestock uses with all formulations;
All indoor uses (except for some stored commodities and storage facilities, and mushroom houses);
All greenhouse uses;
All open-forest land uses;
All seed treatments with all formulations;
All formulations for the following uses:
- Almonds (including hulls and shells)
- Cranberries
- Filberts
- Peanuts (including forage, hay, storage and storage facilities)
- Pea vines (including hay)
- Safflower seed
- Soybeans (including hay and forage)
- Sugar beets
- Sunflower seed
- Treated raisin trays

All pressurized can formulations.

Table 11. Summary of Malathion Occupational Postapplication Restricted Entry Intervals (REIs)

Exposure Scenario	Representative crops	Application Rate (lb ai/acre)	Activity	Days After Treatment (REI)	MOE
Berry, low	blueberries and strawberries	2	hand harvesting, pruning and training	1	120
Field / row crop, low/medium	alfalfa, barley, cotton, flax, forage plants, mint, peas (green and dry), rice and wheat (spring and winter)	2.5	hand harvesting	2	107
			weeding, thinning, irrigation, scouting	0	780
Field / row crop, tall	corn (all types) and sorghum	1.25	hand harvesting (sweet corn), detasseling (seed corn)	4	108
			scouting, irrigating, hand weeding	0	160
Trees, "fruit", deciduous	apples, apricots, cherry, figs, nectarines, peaches and pears	3.75	hand harvesting	3	110
			thinning	5	140
Trees, "fruit", evergreen	avacado, Christmas trees, grapefruit, lemons, mangos, oranges, and papaya	1.25 to 6.25	hand harvesting	3, 6	120, 160
			hand pruning	2, 4	180, 120
Tree, "nut"	macadamia nuts, pecans and walnuts	5	hand harvesting, thinning	4	180
Turf/sod	turf farms and golf courses	8.7	sod harvesting, hand weeding	2	270
ornamentals	nursery crops	2.5	transplant, ball/burlap	5	170
Vegetable, "root"	beets (table), carrots, onions (dry and green), potatoes, sweet potatoes and turnips	1.56	hand harvesting, thinning	2	172
			scouting, irrigating	0	250

Exposure Scenario	Representative crops	Application Rate (lb ai/acre)	Activity	Days After Treatment (REI)	MOE
Vegetable, cucurbit	cantaloupe, cucumbers, squash (summer and winter), watermelon and pumpkin	1.88	hand harvesting, pruning, thinning	2	142
			scouting, irrigating	0	208
Vegetable, fruiting	eggplant, peppers, tomatoes and okra	3.43	hand harvesting, tying, pruning, thinning	1	105
Vegetable, head and stem	broccoli, Brussels sprouts, cabbage and cauliflower	2	hand harvesting, pruning, irrigation	3	124
Vegetable, leafy	celery, collards, kale, lettuce, parsley, spinach, mustard greens, Swiss chard and watercress	2	hand harvesting, pruning, thinning	2	134
Vegetable, stem/stalk	asparagus and pineapple	1.25	hand harvesting, pruning	0, 2	156, 134
		5			
Vine / trellis	blackberries, blueberries, grapes and raspberries	2	cane turning (table grapes)	4	115
			hand harvesting, pruning, thinning	3	124
			tying, training	1	180
Mushrooms	mushrooms	1.7	cutting and harvesting	2	157
Bunch/bundle	hops	0.63	harvesting, pruning, thinning, weeding	0	16