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UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF PREVENTION,
PESTICIDES AND
TOXIC SUBSTANCES

Date: November 8, 1999

MEMORANDUM

SUBJECT: **Malathion**: Preliminary Risk Assessment for the Reregistration Eligibility Decision (RED) Document. Chemical No. 057701. Case No. 0248. Barcode D255364.

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Attached is HED's risk assessment of the insecticide malathion for purposes of issuing a Reregistration Eligibility Decision (RED) Document for this active ingredient. Cumulative risk assessment considering risks from other pesticides or chemical compounds having a common mechanism of toxicity is not addressed in this document. It should be noted that cholinesterase inhibition is not the adverse effect of concern for acute dietary exposure to malathion. When the cumulative exposure assessment for organophosphorous chemicals is conducted, the acute dietary pathway for malathion will be evaluated to determine whether it should be included or excluded from the quantitative cumulative exposure assessment. The disciplinary science chapters and other supporting documents for the malathion RED are also included as attachments as follows:

Re-Evaluation Report of the Hazard Identification Assessment Review Committee. Rowland (12/22/98)
Malathion: Revised NOAEL for Derivation of the Chronic Reference Dose. Rowland (11/1/99)
Combined Report of the HIARC and Safety Factor Committee and its Recommendation for the Organophosphates (August 6, 1998)
Malathion Quantitative Risk Assessment (Q1*). Lori Brunsman (07/13/99)
Product Chemistry Chapter. William O. Smith (06/02/99; D256522)
Residue Chemistry Chapter. William O. Smith (04/14/99; D239453)
Malathion Anticipated Residues. William O. Smith (05/10/99; D255365)
Toxicology Chapter. Brian A. Dementi 03/24/98; D244091)
Occupational and Residential Exposure Assessment. Jack Arthur (09/16/99; D239439)
Preliminary Dietary Risk Assessment (Revised). Richard Griffin (11/03/99)
Incident Report. Jerome Blondell and Monica Spann (08/18/98; D247492)
Malathion Drinking Water Concentrations. Birchfield, et al, (06/10/99; D256746)

HED's Hazard Identification Assessment Review Committee (HIARC) reviewed the toxicological database for malathion and selected toxicological endpoints for acute and chronic dietary and for occupational and residential (dermal and inhalation) exposure risk assessment on November 6, 1997 (memorandum dated December 17, 1997). Following that meeting, the Agency pursued the external review mechanism to address a number of additional issues. The external peer review panel's comments

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were evaluated in HIARC meetings on August 18, 20 and 27, 1998 and are documented in the HIARC's report, Malathion Re-evaluation dated December 22, 1998. On October 28, 1999, the HIARC concluded that the chronic RfD should be revised; the attached risk assessment reflects revision of the chronic RfD. HED's FQPA Safety Factor Committee reviewed the hazard and exposure data for malathion and recommended that the FQPA Safety Factor (as required by Food Quality Act of August 3, 1996) be removed in assessing the risk posed by this chemical (memorandum dated August 6, 1998).

On September 24, October 8, October 15, 1997, June 10, 1998, February 24, 1999 and June 23, 1999, the Health Effects Division's Cancer Assessment Review Committee (CARC) evaluated the carcinogenic potential of malathion. The Committee reviewed the following studies: 1) Carcinogenicity study with malathion in B6C3F1 mice; 2) Combined chronic toxicity/carcinogenicity study with malathion in Fischer 344 rats; and 3) the Combined chronic toxicity/carcinogenicity study with malaoxon in F344 rats. Relevant subchronic, chronic and mutagenicity studies were also reviewed at these meetings, as well as the results of the carcinogenicity studies conducted with malathion and/or malaoxon (during 1978-80) by the National Cancer Institute/National Toxicology Program (NCI/NTP).

At the June 23, 1999 meeting, the Committee classified malathion as a "likely human carcinogen" by majority opinion with the further observation that it is plausible that most tumor occurrences in the rat and mouse studies are dose-limited (i.e., tumors are induced only at excessive doses). Consequently, some members were of the opinion that malathion should be classified as a "suggestive human carcinogen" and that this classification best described the carcinogenic potential for malathion. However, liver tumors in female rats were seen at lower doses, and mode of action studies to demonstrate this hypothesis are not available. The Committee recommended a linear low-dose approach (Q_1^*) for human risk characterization and extrapolation based on the nasal and the liver tumors in rats at all dose levels tested. Since that meeting, a Q_1^* for 1.52×10^{-3} has been calculated for malathion based on female rat liver adenoma and/or carcinomas combined tumors as the most potent unit risk. This slope factor has been used for human health risk assessments in the attached Preliminary Malathion Risk Assessment for the Reregistration Eligibility Decision (RED) Document. The CARC will issue a final report documenting these conclusions. When this report is finalized, the malathion risk assessment will be amended to include detailed information on the carcinogenic classification of malathion in accordance with the Agency's Proposed Guidelines for Carcinogen Risk Assessment (April 10, 1996).

RDI: BRSrSci:ANielsen

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1.0 EXECUTIVE SUMMARY

The Health Effects Division (HED) has conducted a human health assessment for the active ingredient malathion (O,O-dimethyl phosphorodithioate of diethyl mercaptosuccinate) for the purposes of making a reregistration eligibility decision. Only the exposures and risks resulting from Section 3 registrations supported for reregistration are included in this document. A separate risk assessment of malathion use for medfly control under Section 18 Quarantine Exemptions for Florida and California was recently completed by HED (Odiott, et al.; D250394, D249875, D251682).

Malathion is a non-systemic, wide spectrum organophosphorus (OP) insecticide. It is used in the agricultural production of a wide variety of food/feed crops to control insects such as aphids, leafhoppers, and Japanese beetles. Malathion is also used in the Cotton Boll Weevil Eradication Program and as a general wide-area treatment for mosquito-borne disease control. It is also available to the home gardener for outdoor residential uses which include vegetable gardens, home orchards, ornamentals and lawns. The Agency has been informed by the basic producer (Cheminova) and IR4 that certain use sites will not be supported for reregistration. As a consequence, existing product labels permitting indoor uses, direct animal (pet and livestock) treatments, among other uses, are not addressed in this risk assessment.

Malathion is formulated as a technical (91-95% ai), a dust (1-10% ai), an emulsifiable concentrate (3-82%) ai, a ready-to-use (1.5-95% ai), a pressurized liquid (0.5-3% ai), and a wettable powder (6-50% ai). Several of the 95% liquids are intended for ultra-low-volume (ULV) applications. Malathion can be applied using ground or aerial equipment, thermal and non-thermal fogger, ground boom, airblast sprayer, chemigation, and a variety of hand-held equipment such as backpack sprayers, low pressure handwands, hose-end sprayers, and power dusters. Multiple foliar applications may be made as needed depending on pest presence at application rates ranging from 0.1 to 8.7 lb ai/A.

Cheminova Agro summarized malathion usage in four major market areas and provided the following market share information: USDA Boll Weevil and other special program uses (59-61%), general agriculture uses (16-20%), public health uses (8-15%), and home and garden uses (10%). Based on available pesticide survey information from EPA's Biological and Economics Assessment Division reflecting total lb ai used per year for the period 1987 to 1996, the most predominant agricultural use of malathion is on cotton (36%) followed by cereal grains (12%), alfalfa (10%), small fruits and berries (about 9%), pome and stone fruits (4%), and tree nuts (3%).

Malathion is an OP insecticide, and like all members of this class, the mode of toxic action is the inhibition of cholinesterase (ChE). The selective toxicity of malathion has been well documented. Malathion is metabolically converted to its structurally similar metabolite, malaoxon (oxidation of the P=S moiety to P=O), in insects and mammals. Both malathion and malaoxon are detoxified by carboxyesterases leading to polar, water-soluble, compounds that are excreted. Mammalian systems show greater carboxyesterase activity, as compared with insects, so that the toxic agent malaoxon builds up more in insects than in mammals. This accounts for the selective toxicity of malathion towards insects. In humans, the metabolism of malathion results in either detoxification (hydrolysis of malathion to monocarboxylic acids) or the production of malaoxon. In rats, malaoxon exhibits approximately 10 to 30 times greater acute oral toxicity than malathion.

Relative to other OP insecticides, malathion exhibits low acute oral toxicity in tests with technical material; and, unlike other OPs where acute dietary NOAELs have been established based on cholinesterase inhibition, the acute dietary NOAEL for malathion is based on maternal toxicity in a developmental toxicity study characterized by reduced mean body weight gain. With this exception, all other endpoints selected for malathion risk assessment were based on cholinesterease inhibition. Other treatment related effects of malathion via inhalation exposures were histopathologic lesions of the nasal cavity and larnyx. Via oral

exposures, increased incidences of liver and nasal tumors were observed in rats and increased incidence of liver tumors were observed in mice. Malathion is carcinogenic in both the rat (inducing liver and nasal tumors) and the mouse (inducing liver tumors).

Malaoxon, the active cholinesterase inhibiting metabolite of malathion was not carcinogenic in rats. The only clinical sign that appeared to be treatment related was the increase in yellow anogenital staining seen during the last 6 months of treatment. Decreased body weight and body weight gains were considered to be treatment-related, and plasma, red blood cell (RBC), and brain ChE inhibition was dose-related and statistically significant at most time points (3, 6, 12 and 24 months) during the two-year study.

HED evaluated the toxicological, residue chemistry, and exposure data bases for malathion and malaoxon and determined that the data are adequate to support a reregistration eligibility decision. In assessing aggregate risk, HED considered potential dietary exposure of the general population to malathion residues from food and drinking water, and potential dermal and inhalation exposure from use in residential settings. HED also considered dermal and inhalation exposure to occupational pesticide handlers, mixers, loaders, applicators and postapplication dermal exposure to workers during harvesting activities.

With the exception of acute (single dose) dietary exposure, the toxicity endpoints selected for risk assessment are based primarily on neurotoxic effects of cholinesterase (ChE) inhibition in the brain, RBC and plasma. A dose level of 2.4 mg/kg/day (repeated oral doses) was selected for chronic dietary risk assessment. A dose level of 50 mg/kg/day (compiled from main and range-finding studies) was selected for acute dietary risk assessment; effects were reduced mean body weight gain. Dose levels of 50 mg/kg/day (21-day dermal dose) were selected for both short- and intermediate-term occupational and residential risk assessment, while a dose level of 25.8 mg/kg/day (90-day inhalation dose) was selected for assessment of occupational and residential inhalation risk during any exposure duration. For assessment of long-term dermal risk, a dose level of 2.4 mg/kg/day (repeated oral doses), and a dermal absorption factor of 10% was selected. In combined chronic toxicity/carcinogenicity studies, increased incidence of liver tumors was observed in rats and mice and increased incidence of nasal tumors was seen only in rats.

An uncertainty factor (UF) of 100 was applied to all doses selected for risk assessment purposed to account for interspecies extrapolation (10x) and intraspecies variability (10x). An additional UF of 10x was applied to the dose selected for inhalation risks because a NOAEL was not identified and because of the severity of the nasal lesions observed in a range finding study. The 10x FQPA safety factor was removed for all populations.

For assessment of cancer risk, a linear low-dose approach (Q_1^*) was used for human risk characterization and extrapolation. The unit risk was calculated at 1.52×10^{-3} in human equivalents based on female rat liver adenoma and/or carcinoma combined tumor rates. This Q_1^* was used for assessing cancer risk for all routes of exposure (oral, dermal and inhalation).

For assessment of non-cancer risk, malathion and malaoxon were considered toxicologically equivalent; however, for assessment of cancer risk only malathion exhibited carcinogenic potential.

HED conducted acute and chronic dietary (food) exposure analyses using the Dietary Exposure Evaluation Model (DEEM). In both assessments, exposure (residue x consumption) was compared to a population adjusted dose (PAD) reflecting removal of the FQPA 10x factor. The PAD is equal to the acute or chronic RfD divided by the FQPA Safety Factor. HED considers dietary residue contributions greater than 100% of the PAD of concern. **Acute dietary** exposure at the 95th percentile comprised 20% of the aPAD for the general population and 38% of the aPAD for the most highly exposed subgroup, children (1-6 years). The acute analysis at the 95th percentile is a conservative, deterministic upper-bound estimate

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which utilized tolerance-level input residues and assumed 100% crop treated. A refinement of this high-end acute dietary exposure assessment was not conducted because cholinesterase inhibition is not the adverse effect of concern for acute dietary exposure to malathion. When the cumulative exposure assessment for organophosphorous chemicals is conducted, the acute dietary pathway for malathion will be evaluated to determine whether it should be included or excluded from the quantitative cumulative exposure assessment. **Chronic dietary** exposure comprised 2% of the cPAD for the general population and 4% of the cPAD for the most highly exposed subgroup, children (1-6 years). **Carcinogenic** risk for malathion in the food supply is estimated to be 5.8×10^{-7}. The chronic exposure analysis (Tier 3) was incorporated into both chronic (non-cancer) and carcinogenic risk assessments. This analysis is a refined estimate which used USDA/PDP and FDA monitoring data, average field trial residues and percent of crop treated data.

The available environmental fate data on malathion indicate that it is extremely mobile and shows little persistence in soil and water. The primary route of dissipation of malathion in surface soils appears to be aerobic metabolism. Limited fate data are available for the degradate malaoxon. However, based on its chemical similarity to malathion, the parent and its degradate are expected to have similar chemical properties. Malathion and its degradates in general are soluble and do not adsorb strongly to soils. The Environmental Fate and Effects Division (EFED; Birchfield and Birchfield et al.) provided an analysis of available ground water monitoring data and a screening-level assessment using simulation models to estimate the potential concentration of malathion and its degradate malaoxon in surface water.

EFED conducted screening-level model estimates of malathion and malaoxon concentrations in surface water using GENEEC. The estimated environmental concentrations (EEC) of combined malathion and malaoxon in surface water were **322 μg/L and 97 μg/L**, representing peak and average levels, respectively. EFED also conducted a Tier II screening-level assessment of malathion per se in surface water using PRZM-EXAMS which predicted a multi-year mean of **4 μg/L.** The calculated drinking water levels of comparison (DWLOCs) as a contribution of acute and chronic aggregate exposures are **3,100 and 232 μg/L,** respectively, for the most highly exposed population subgroup, children age 1-6 years. The cancer DWLOC for the U.S. population is **10 μg/L.**

Occupational and non-occupational (residential) exposure to malathion and malaoxon residues via dermal and inhalation routes can occur during handling, mixing, loading, and applying activities. Postapplication exposure potentials also exist. There is potential dermal exposure to persons entering treated sites (occupational and non-occupational) following application of malathion-containing products. There is also potential for dermal and inhalation exposure to individuals (bystanders) contacting lawns at home or in public areas from aerial or ground applications for mosquito control.

Based on toxicological criteria and potential for exposure, HED has conducted dermal and inhalation exposure assessments for the occupational and residential handler, as well as occupational and residential postapplication dermal and inadvertent oral ingestion exposure to adults and/or children. The duration of exposure is expected to be short- and intermediate-term for the occupational handler and short-term for the residential handler. The Pesticide Handler's Exposure Database (PHED) and the Standard Operating Procedures (SOPs) for Residential Exposure Assessments (December, 1997) were used as data sources and methods of estimating occupational and residential exposures.

Dermal and inhalation exposure assessments for occupational handlers involved in mixing/loading and/or applying malathion were conducted by HED using a range of application rates and frequency of use from current product labels, the PHED Version 1.1 database, and standard assumptions regarding average body weight, work day intervals, and daily amount handled (acres treated/day or volume used/day). For non-cancer risk assessment, aggregate risk indices (ARIs) were used to combine dermal and inhalation Margins of Exposure (MOEs). This index normalizes all uncertainty factors to one; an ARI of less than

one is indicative of a risk concern. For cancer risk assessment, dermal and inhalation exposures were converted to oral equivalents and risk estimates were calculated using the oral Q_1^* of 1.52×10^{-3} $(mg/kg/day)^{-1}$. Postapplication risks were estimated using dislodgeable foliar residue (DFR) data and HED's standard transfer coefficients to estimate residue transfer for crop/activity patterns. Initial DFR values were derived using 1.3% of the application rate for turf (turf dissipation study) and 20% of the application rate for all other crops (HED's standard value). A dissipation rate of 46% per day (rather than HED's standard value of 10% per day) was used for all crops and activities.

Occupational Short- and Intermediate-Term Risk Summary: Combined dermal and inhalation exposures to handlers are of risk concern for only one scenario (applying sprays with an airblast sprayer [ag fruit & nut]) despite the maximum mitigation measures. The ARI for this scenario is 0.94; thus, the risk concern may be moderated due to the closeness of the risk estimate to the target ARI. Using baseline attire, combined dermal and inhalation risks to handlers are not of concern for about one-third of the 16 major exposure scenarios (ARIs range from 1 to 48). With the addition of PPE and engineering controls to mitigate risk concerns for the remaining scenarios, ARIs ranged from 1 to 29.

Occupational postapplication risk is of concern for reentry on the same day as application (12 hours following treatment) for all exposure scenarios except for non-harvesting activities associated with crops for which there is potential for a low degree of dermal contact (e.g., asparagus, broccoli and soybeans) at the 0.5 lb ai/acre rate, and for all non-harvesting reentry activities associated with mowing and maintaining turfgrass. Postapplication risks were estimated using chemical specific dislodgeable residue data, where applicable, and standard transfer coefficients (TCs). Restricted Entry Intervals (REIs), where the margins of exposure are NOT of concern for workers, are estimated to range from 1 to 6 days. Because crops treated with malathion have an existing REI of 12 hours, HED has a concern over occupational short- and intermediate-term occupational postapplication risk.

Occupational Cancer Risk Summary: Cancer risk estimates for occupational dermal and inhalation exposure are not greater than or are approximately equal to 1.0×10^{-6} for all scenarios when the necessary mitigation measures are applied.

Occupational postapplication risk is of concern for reentry on the same day as application (12 hours following treatment) for all exposure scenarios except for non-harvesting activities associated with crops for which there is potential for a medium degree of dermal contact at the 0.5 lb ai/acre rate; non-harvesting activities associated with crops for which there is a low degree of dermal contact (e.g., asparagus, broccoli and soybeans) at the 0.5 lb ai/acre rate, and for non-harvesting activities associated with mowing and maintaining turfgrass. Because crops treated with malathion have an existing REI of 12 hours, HED has a concern over occupational postapplication cancer risk. However, short- and intermediate-term toxicity endpoints drive the ultimate determination of postapplication risk and reentry intervals for malathion, not the cancer risk described above.

Residential Non-cancer Risk Summary: Residential handler risk estimates exceed HED's level of concern. Three of the five short-term residential handler exposure scenarios result in ARIs (based on typical or maximum usage rates) ranging from 0.02 to 0.7 that exceed HED's level of concern defined by a target ARI of 1. Residential postapplication exposures also exceed HED's level of concern. Postapplication dermal MOEs are ≤36 (adults and toddlers) from contact with commercially treated turf and ≤63 (adults) from contact with vegetables/small fruit gardens, fruit trees, and ornamentals following homeowner spray applications and in "pick-your-own" strawberries. MOEs for all other scenarios substantially exceed the target MOE of 100 (600 to

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>860,000) and are not of risk concern. Public health uses (ground and aerial ULV application) result in dermal MOEs that are >3,400 for toddlers and adults and incidental oral ingestion MOEs that are >25,000 for toddler's hand(object)-to-mouth activities.

Residential Cancer Risk Summary: With the exception of the shaker can uses, cancer risk estimates for residential handlers are in the **10^{-7} to 10^{-9}** range and do not exceed HED's level of concern. The shaker can uses are of risk concern: handler dermal exposure alone results in a cancer risk estimates in the **10^{-5} range**. Residential postapplication exposures also exceed HED's level of concern. Postapplication dermal contact with turf following treatment by handgun application, contact with vegetables and small fruit gardens, and contact from "pick-your-own" strawberries all have risk estimates slightly above 1 $x10^{-6}$. Dermal postapplication exposure from contacting turf following aerial or ground-based ULV mosquito control is well below 1 $x10^{-6}$, as is contact with treated fruit trees and ornamentals.

Aggregate risk estimates for adults and children considered exposure to malathion through dietary (food and water) sources. Although there are a number of other non-occupational sources (residential) such as 1) outdoor use of malathion-containing consumer products by residential handlers; 2) commercial use of malathion at residential sites, "pick-your-own" strawberries or other orchards, public access areas such as parks, golf courses, recreational areas, and playgrounds; and 3) public health use of malathion for wide area mosquito control, these were not included in aggregate short-term and cancer risk estimates.

Aggregate acute risk estimates do not exceed HED's level of concern. The aggregate acute dietary risk estimates include exposure to combined residues of malathion and malaoxon residues in food and water and does not include dermal and incidental oral exposure. Acute dietary exposure from food is 38% of the acute PAD for the most highly exposed population subgroup (children 1-6 years) and does not exceed HED's level of concern. Using conservative screening-level models, the estimated environmental concentrations of malathion and malaoxon in surface and ground water were less than the acute drinking water level of comparison, indicating that acute aggregate exposure to malathion does not exceed HED's level of concern. Based on the available information, HED concludes with reasonable certainty that no harm to any population will result from acute aggregate dietary exposure to malathion.

Aggregate Short-term risk estimates were not conducted because the Aggregate Risk Indices (ARIs) for residential dermal and inhalation exposure exceed HED's level of concern for several residential handler scenarios and for several residential postapplication (adult and toddler) scenarios. Any additional exposure through food and water would further contribute to the existing risk concern for adult and toddler residential exposure.

Aggregate chronic (non-cancer) risk estimates do not exceed HED's level of concern. The aggregate chronic dietary risk estimates include chronic exposures to combined residues of malathion and malaoxon in food and water. No chronic residential use scenarios were identified. Chronic dietary exposure is 4% of the chronic PAD for the most highly exposed population subgroup (children 1-6 years) and does not exceed HED's level of concern. The estimated environmental concentrations in ground and surface water are less than the drinking water level of comparison, indicating that chronic aggregate exposure to malathion does not exceed HED's level of concern. Based on the available information, HED concludes with reasonable certainty that no harm to any population will result from chronic aggregate dietary exposure to malathion.

Aggregate carcinogenic risk estimates were not conducted because risk to adults from residential dermal and inhalation exposure alone exceed HED's level of concern for several

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handler and postapplication exposure scenarios. Any additional exposure through food and water would further contribute to the existing risk concern for adult residential exposure.

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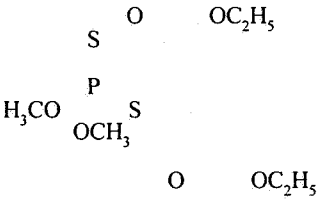
2.0 PHYSICAL/CHEMICAL PROPERTIES CHARACTERIZATION

2.1 Identification of Active Ingredient - Malathion

Chemical Name:	O,O-dimethyl dithiophosphate of diethyl mercaptosuccinate
Chemical Group:	Organophosphate
Chemical Type:	Insecticide
CAS Registry No.:	121-75-5
Common Name:	Malathion
PC Code Number:	057701
Mode of Action:	Cholinesterase inhibition
Empirical Formula:	$C_{10}H_{19}O_6PS_2$
Molecular Weight:	330.4
Appearance:	Colorless, yellow, amber, or brown
Boiling Point:	156-157 C
Vapor Pressure:	0.00004 mmHg at 30 C
Solubility:	145 ppm at 25 C in water; readily soluble in most alcohols, esters, aromatic solvents, and ketones, and is only slightly soluble in aliphatic hydrocarbons
Half-life:	T½ = 3 days (used for EEC modeling)
Toxic Impurities:	A number of impurities (e.g. isomalathion) have been reported to be present in representative technical formulations of malathion. Currently available data in support of reregistration, indicates that potential impurities and degradates are found either to be less toxic than the parent or the malaoxon, or are present at levels which do not pose a residue concern.

2.2 Structural Formula of Malathion



2.3 Identification of Active Ingredient - malaoxon

Only limited information is available for characterization of the physical/chemical properties of the malaoxon. The following information was obtained in part from Chemical Abstracts:

Chemical Name:	O,O-dimethyl thiophosphate of diethyl mercaptosuccinate
CAS Registry Number.:	1634-78-2
Common Name:	Malaoxon
Empirical Formula:	$C_{10}H_{19}O_7PS$
Molecular Weight:	314.29
Vapor Pressure:	2.45E-06 to 3.2E-04 torr at 10.0 to 50.0 C
Half-Life:	T½ = 21 days (used for EEC modeling)

3.0 HAZARD CHARACTERIZATION

3.1 Hazard Profile

The toxicity database for malathion is substantially complete and of acceptable quality to assess the potential hazard to humans, including special sensitivity of infants and children. The database will support a reregistration eligibility determination for the currently registered uses. However, two new toxicity studies have been required to fully comply with guideline requirements and to provide better hazard characterization: 1) a 90-day feeding study in dogs because the available 1-year study is unacceptable, and 2) a 90-day inhalation study in rats because the available 90-day study did not establish a NOAEL. In addition, the Agency has recently issued FR42945 (August 6, 1999) requiring registrants of neurotoxic pesticides to conduct acute, subchronic, and developmental neurotoxicity studies. Thus, a developmental neurotoxicity study for malathion will be required under this Data Call-in program. Tables 1 through 8 present the toxicity profile for malathion.

Malathion is an organophosphorus (OP) insecticide, and like all members of this class, the mode of toxic action is the inhibition of cholinesterase (ChE). However, relative to other OP insecticides, malathion exhibits low acute oral toxicity in tests with technical material; and, unlike other OPs where acute dietary NOAELs have been established based on cholinesterase inhibition, the acute dietary NOAEL for malathion is based on maternal toxicity characterized by reduced mean body weight gain. With this exception, all other endpoints selected for malathion risk assessment were based on cholinesterease inhibition. Other treatment related effects of malathion via inhalation exposures were histopathologic lesions of the nasal cavity and larnyx. Via oral exposures, increased incidences of liver and nasal tumors were observed in rats and increased incidence of liver tumors were observed in mice. Malathion is carcinogenic in both the rat (inducing liver and nasal tumors) and the mouse (inducing liver tumors). The linear low-dose approach (Q_1*) was used for human risk characterization. The Q_1* calculated for risk assessment is 1.52×10^{-3} $(mg/kg/day)^{-1}$ based on combined liver adenomas and/or carcinomas in female rats. This Q_1* was used for assessing cancer risk for all routes of exposure (oral, dermal and inhalation).

For assessment of non-cancer risk, malathion and malaoxon were considered toxicologically equivalent; however, for assessment of cancer risk only malathion exhibited carcinogenic potential.

3.2 Toxicity Profile

3.2.1 Acute Toxicity

Malathion exhibits low acute toxicity via the oral, dermal, and inhalation routes (Toxicity Category III or IV). It exhibits only slight eye and dermal irritation and is not dermally sensitizing. Details of acute toxicity testing with technical grade malathion are presented in Table 1.

It would be useful to compare CSFs to determine what differences there are in product composition between the test material used in the acute studies and the technical product now marketed.

Table 1. Acute Toxicity of Technical Malathion (97.4% a.i.).

Test and Species	Results	MRID (Date)	Toxicity Category
Acute Oral - Rat	LD50 = 5400 mg/kg (M) LD50 = 5700 mg/kg (F)	00159876 (1986)	IV
Acute Dermal - Rat	LD50 > 2000 mg/kg (M) (F)	00159877 (1986)	III
Acute Inhalation - Rat	LC50 > 5.2 mg/L (M) (F)	00159878 (1986)	IV
Primary Eye Irritation - Rabbit	Slight conjunctival irritation; cleared by 7 days.	00159880 (1985)	III
Primary Skin Irritation - Rabbit	Slight dermal irritation (PIS = 1.1)	00159879 (1985)	IV
Dermal Sensitization - Guinea Pig	Not dermally sensitizing	00159881 (1986)	-

Although no acute toxicity test data for malaoxon have been submitted, data available from published literature (Dauterman and Main, 1966) indicate that the acute oral LD50 for malaoxon is 158 mg/kg/day in rats. Based on a comparison of the malaoxon oral LD50 value from this study with the LD50 for malathion from a guideline study, malaoxon appears to be approximately 10 to 30 times greater acute oral toxicity than malathion in rats.

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3.2.2 Subchronic Toxicity

In subchronic studies with malathion, plasma and RBC cholinesterase inhibition were exhibited at the LOAEL in both rabbits and rats following dermal and inhalation exposure and brain cholinesterase inhibition in female rabbits following dermal exposure. Brain cholinesterase inhibition occurred at higher doses in both species. No clinical signs or other treatment-related effects were observed in dermally treated rabbits. Both clinical signs and treatment-related microscopic lesions of the nasal cavity and larnyx were observed in rats following inhalation exposure in whole body exposure chambers.

Table 2. Subchronic Toxicity of Malathion

Guideline	Study Type (Test Material)	MRID (Date)	RESULTS
870.3200 82-2	21-day dermal-rabbit **(Malathion technical 94% a.i.)**	41054201 (1988)	ChEI NOAEL: 50 mg/kg/day ChEI LOAEL: 300 mg/kg/day, based on plasma and RBC cholinesterase inhibition in males; and plasma, RBC, and brain cholinesterase inhibition in females.
870.3465 82-4	90-day inhalation-rat **(Malathion technical 96.4% a.i.)**	43266601 (1994)	Systemic NOAEL: not established Systemic LOAEL: 0.1 mg/L (LDT), based on histopathologic lesions of the nasal cavity and larnyx in males and females. ChEI NOAEL: not established ChEI LOAEL: 0.1 mg/L (LDT), based on plasma and RBC cholinesterase inhibition in females

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3.2.3 Chronic Toxicity/Carcinogenicity

The Agency has spent considerable time and effort on evaluation and interpretation of the chronic toxicity/carcinogenicity data for malathion and malaoxon. HED's Cancer Assessment Review Committee (CARC) has met on six occasions since September 24, 1997 to evaluate the carcinogenic potential of malathion. The following studies were reviewed during this period: 1) combined chronic toxicity/carcinogenicity study in Fisher 344 rats with malathion; 2) carcinogenicity study in B6C3F1 mice with malathion; and 3) combined chronic toxicity/carcinogenicity study in Fisher 344 rats with malaoxon. The CARC also considered the results of the 1978-80 studies conducted with malathion or malaoxon by the National Cancer Institute/National Toxicology Program. The deliberations of the CARC have given thorough consideration to comments provided by EPA staff and others regarding the CARC's consensus interpretation of the scientific evidence presented in the above studies.

Evidence for carcinogenicity was demonstrated by the presence of liver tumors in male and female B6C3F1 mice as well as liver tumors in female Fischer 344 rats and nasal tumors in male and female Fischer 344 rats. The CARC concluded that there is evidence of carcinogenicity in both sexes of mice at the two highest dose levels tested (8,000 and 16,000 ppm). There is no statistically significant evidence of carcinogenicity in male or female mice at the lower levels tested (100 and 800 ppm). In female rats, the occurrence of two liver tumors per dose level at 50 and 500 ppm (dose levels considered to be not excessive) was considered to be of biological significance. The CARC concluded that the incidence of liver tumors in female rats at 50 and 500 ppm provided suggestive evidence of carcinogenicity and that the incidences of liver tumors at 6,000 and 12,000 ppm (although 12,000 ppm is considered to be an excessive dose) provided positive evidence of carcinogenicity. In female rats, there was one adenoma of the respiratory epithelium at 6,000 ppm and one at 12,000 ppm compared to none in the controls. The CARC recommended a linear low-dose extrapolation model (Q_1^*) be used for human risk characterization. The Q_1^* calculated for risk assessment is 1.52×10^{-3} $(mg/kg/day)^{-1}$ for combined female rat liver adenoma and/or carcinomas in 3/4's human equivalents.

Malaoxon, the active cholinesterase inhibiting metabolite of malathion was not carcinogenic in rats. The only clinical sign that appeared to be treatment related was the increase in yellow anogenital staining seen during the last 6 months of treatment. Decreased body weight and body weight gains were considered to be treatment-related, and plasma, RBC, and brain ChE inhibition was dose-related and statistically significant at most time points (3, 6, 12 and 24 months) during the two-year study. A NOAEL for ChEI was not established; RBC cholinesterase inhibition in males and females was observed at the LOAEL of 1 mg/kg/day after 6 months of treatment.

The chronic toxicity/carcinogenicity profile of malathion and malaoxon is given in Table 3.

Table 3. Chronic Toxicity/Carcinogenicity of Malathion and Malaoxon.

Guideline	Study Type (Test Material)	MRID (Date)	RESULTS
Chronic Toxicity/Carcinogenicity of Malathion			
870.4300 83-5	Combined chronic toxicity/ carcinogenicity-F344 rats **(Malathion technical 97.1% a.i.)** Dose levels: 0, 50 ppm (2.4 mg/kg/d) 100/50 ppm (3.14♂/3.8♀ mg/kg/d), 500 ppm (26♂/32♀ mg/kg/d), 6,000 ppm (327♂/386♀ mg/kg/d), 12,000 ppm (677♂/817♀ mg/kg/d)	43942901 (1996)	ChEI NOAEL: 2.4 mg/kg/day ChEI LOAEL: 29 mg/kg/day, based on significant plasma cholinesterase inhibition in males at 24 months. Increased incidence of liver tumors in female rats and increased incidence of nasal tumors in male and female rats.
870.4200 83-2b	Carcinogenicity-B6C3F1 mice **(Malathion technical 96.4% a.i.)** Dose levels: 0, 100 ppm (17.4♂/20.8♀ mg/kg/d), 800 ppm (143♂/167♀ mg/kg/d), 8,000 ppm (1476♂/1707♀ mg/kg/d), 16,000 ppm (2978♂/3448♀ mg/kg/d).	43407201 (1994)	Systemic NOAEL: 143♂/167♀ mg/kg/day Systemic LOAEL: 1,476♂/1,707♀ mg/kg/day, based on decreased body weights and food consumption, increased liver weight, and increased hepatocellular hypertrophy in males and females. ChEI NOAEL: 17.4♂/20.8♀ mg/kg/day CHEI LOAEL: 143♂/167♀ mg/kg/day, based on plasma and RBC cholinesterase inhibition in males and females. Increased incidence of liver tumors in male and female mice.
Chronic Toxicity/Carcinogenicity of Malaoxon			
870.4300 83-5	Combined chronic toxicity/ carcinogenicity-F344 rats **(Malaoxon technical 96.4% a.i.)** Dose levels: 0, 20 ppm (1 mg/kg/d), 1,000 ppm (57♂/68♀ mg/kg/d), 2,000 ppm (114♂/141♀ mg/kg/d).	43975201 (1996)	Systemic NOAEL: 1 mg/kg/day Systemic LOAEL: 57♂/68♀ mg/kg/day based on increased mortality and microscopic changes in the nasal tissue, lung interstitium, and tympanic cavity in females and increased incidences of mineral deposits in the stomach muscularis in males. ChEI NOAEL: Not established ChEI LOAEL: 1 mg/kg/day based on RBC cholinesterase inhibition in males and females after 6 months of treatment. No evidence of carcinogenicity in male or female rats.

On October 28, 1999, HIARC evaluated the mean compound intake in the combined chronic toxicity/carcinogenicity study in rats (43942901) and its impact on the derivation of the chronic reference dose. The mean test substance intake for rats of both sexes at all dose was recalculated using periodic test substance intake data and these calculations confirm that test compound intakes are actually somewhat lower than those previously estimated. The HIARC concluded that the chronic RfD should be based on the NOAEL of 2.4 mg/kg/day and the UF of 100 yielding a chronic RfD of 0.024 mg/kg/day.

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3.2.4 Developmental Toxicity Studies

Malathion was evaluated for developmental toxicity in rats and rabbits. In rabbits, developmental effects (slightly increased incidence of mean resorption sites per dam) were noted at 50 mg/kg/day where maternal toxicity was also observed. No developmental effects were noted in rats at the highest dose tested (800 mg/kg/day). Maternal toxicity (cholinergic signs and reduced mean body weights) were observed in both species. A summary of the developmental studies for malathion is given in Table 4.

Table 4. Developmental Toxicity of Malathion

Guideline	Study Type (Test Material)	MRID (Date)	RESULTS
870.3700 83-3	Developmental Toxicity-Rat **(Malathion technical 94% a.i.)**	41160901 (1989)	Maternal NOAEL: 400 mg/kg/day Maternal LOAEL: 800 mg/kg/day, based on reduced mean body weight gains and reduced mean food consumption. Developmental NOAEL: 800 mg/kg/day Developmental LOAEL: >800 mg/kg/day; no adverse developmental effects were observed at the highest tested dose.
870.3700 83-3	Developmental Toxicity-Rabbit (main study) **(Malathion technical 92.4% a.i.)**	40812001 (1985)	Maternal NOAEL: 25 mg/kg/day Maternal LOAEL: 50 mg/kg/day, based on reduced mean body weight gains in does during the dosing period. Developmental NOAEL: 25 mg/kg/day Developmental LOAEL: 50 mg/kg/day based on a slightly increased incidence of mean resorption sites per dam.
870.3700 83-3	Developmental Toxicity-Rabbit (range-finding) **(Malathion technical 92.4% a.i.)**	00152569 (1985)	Maternal NOAEL: 100 mg/kg/day Maternal LOAEL: 200 mg/kg/day based on mortality and clinical signs of toxicity attributable to multiple doses. Developmental NOAEL: 400 mg/kg/day Developmental LOAEL: >400 mg/kg/day; upon external examination (only), no gross abnormalities were observed at the highest tested dose.

It should be noted that a dose level of 50 mg/kg/day was selected for acute dietary risk assessment. This dose level was compiled from main and range-finding developmental toxicity studies in the rabbit. Toxicological endpoints (e.g., death, clinical signs, or certain developmental abnormalities) attributable to a ***single*** oral dose were not observed in does at 50 mg/kg/day. Although 50 mg/kg/day was a LOAEL for the study for maternal toxicity as a consequence of multiple dosing, HIARC concluded that it would not have been an effect level for maternal toxicity following a single dose.

3.2.5 Reproduction Studies

Malathion did not induce reproductive toxicity in rats at the highest dose tested. Although the offspring NOAEL was lower than the parental systemic NOAEL, pup body weight decrements were primarily observed at postnatal day 21. At that time, young rats consume approximately twice the diet per unit body weight than do adult rats. Thus, the test substance intake by these animals is likely to be more than double the adult intake because of the ingestion of the test material both via the milk (lactation) and food. Table 5 summarizes the reproduction study for malathion.

Table 5. Reproductive Toxicity of Malathion.

Guideline	Study Type (Test Material)	MRID (Date)	Results
870.3800 83-4	2-Generation Reproduction Toxicity-Rats **(Malathion technical 94% a.i.)**	41583401 (1997)	Parental NOAEL: 394♂/451♀ mg/kg/day Parental LOAEL: 612♂ /703♀ mg/kg/day, based on decreased F0 generation body weights during gestation and lactation and decreased F1 pre-mating body weights. Offspring NOAEL: 131♂ /153♀ mg/kg/day Offspring LOAEL: 394♂ /451♀ mg/kg/day, based on decreased pup body weights during the late lactation period in F1 and F2 pups.

3.2.6 Mutagenicity Studies

As shown in Table 6, results of three guideline genetic toxicology studies with malathion indicate that the test material did not cause gene mutations in bacteria or unscheduled DNA synthesis (UDS) in cultured rat hepatocytes. Similarly, malathion was neither clastogenic nor aneugenic up to doses that showed clear cytotoxicity for the target tissue *in vivo*. By contrast, studies from the open literature indicated that malathion is a confirmed clastogen both *in vitro* and *in vivo*. However, there are uncertainties regarding the relevance of these findings to a possible mutagenic mode of action for malathion since positive results from both *in vivo* and *in vitro* studies were seen only at cytotoxic doses and/or the types of induced aberrations were asymmetric and, therefore, not consistent with cell survival. Nevertheless, malathion was shown to be weakly reactive with DNA and does contain a structure that suggests electrophilicity. The CARC concluded, therefore, that while the evidence for mutagenicity as an influence on the tumorigenicity of malathion is weak, at this time, it can not be ruled out.

The overall assessment of studies from the open literature indicated that there is overwhelming evidence that malathion is genotoxic, producing structural damage to chromosomes *in vitro* and in whole animal studies with mice and hamsters. Similar conclusions were reached by Flessel *et al.*, (1993) in the genetic toxicology review prepared for the California Department of Health Services. It should be noted, however, that while 5 of 7 *in vivo* bone marrow studies were reported positive, evidence of structural chromosome damage was either accompanied by cytotoxicity (i.e., significantly reduced mitotic indices or increased cell cycle delay) or asymmetrical structural aberrations (i.e., chromatid and chromosome breaks and exchanges). A similar observation regarding cytotoxicity and the induction of unstable aberrations, which generally lead to death and hence do not directly contribute to carcinogenesis, can also be made for the 5

of 7 positive *in vitro* cytogenetic assays. Nevertheless, the review prepared by Flessel *et al.*, also indicated evidence of malathion's *in vitro* interaction with DNA. Weak but positive results were shown for sister chromatid exchange induction and methylation and denaturation of DNA. Moreover, the methyl ester moiety of malathion is listed by Ashby and Tennant (1991) as a structural alert to DNA reactivity. No assays with germinal cells have been submitted to the Agency. However, malathion was negative in *Drosophila melanogaster* sex linked recessive lethal assays, mouse dominant lethal assays and spermatogonia and/or spermatocyte cytogenetic assays. An adverse heritable effect has not been suggested for malathion.

No mutagenicity studies have been submitted to the Agency on the major metabolite of malathion, malaoxon. The consensus opinion from reviews of the open literature is that malaoxon is not mutagenic in bacteria but is a confirmed positive without S9 activation in the mouse lymphoma assay forward gene mutation assay. Malaoxon was not clastogenic in cultured Chinese hamster ovary (CHO) cells; however, the findings from the mouse lymphoma assay suggest that malaoxon may induce both gene mutations and chromosome aberrations. Nonactivated malaoxon also caused SCEs in independently performed investigations with CHO cells. Malaoxon has the same structural alert that was identified by Ashby and Tennant (1991) for malathion.

Table 6. Mutagenicity Studies with Malathion.

Guideline	Study Type	MRID (Date)	Results
870.5100 84-2	Gene mutation: *Salmonella typhimurium/ Escherichia coli*	40939302 (1987)	**Negative** at all tested concentrations up to 5,000 μg/plate with and without S9 metabolic activation.
870.5385 84-2	Chromasome Aberration: *in vivo* bone marrow assay, rats	41451201 (1990)	**Negative** in *in vivo* bone marrow cytogenetic assay at doses up to clinically and cytotologically toxic levels (2,000 mg/kg).
870.5550 84-2	Unscheduled DNA Synthesis Primary rat hepatocytes	41389301 (1989)	**Negative** in *in vitro* primary rat hepatocytes for induction of UDS at doses up to cytotoxic levels (150-200 μg/mL).

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3.2.7 Neurotoxicity Studies

Neurotoxicity studies are designed to identify acute, subchronic and/or delayed neurotoxic effects. While all chemicals are evaluated for major neurobehavioral and neuropathological effects in the acute and subchronic neurotoxicity screening batteries in rats; organophosphates are also evaluated for delayed neurotoxicity in adult hens.

The neurotoxicity of malathion was evaluated in the acute and subchronic neurotoxicity studies in the rat and the acute delayed neurotoxicity study in the hen. All studies were found to be acceptable and satisfied the appropriate guideline requirements. A detailed summary of these study results is presented in Table 7.

The acute delayed neurotoxicity study in the hen did not reveal any treatment-related findings at gross necropsy nor histopathological examination in hens. Further, malathion was negative for any evidence of acute delayed neurotoxicity.

The acute and subchronic neurotoxicity studies were performed up to or exceeding the limit dose (acute, 2000 mg/kg; subchronic, 1000 mg/kg/day); in the acute study the LOAEL was established at the limit dose. Even though malathion is an organophosphorous compound, effects at the LOAEL were not solely based on the inhibition of cholinesterase. For the acute study, evaluations at the peak time of effect on day 1 (15 min post dosing) revealed decreased motor activity in males and clinical signs (salivation, urogenital staining) in both sexes. Inhibition of plasma and RBC, but not brain, cholinesterase were observed in high-dose animals. At day 7, plasma and RBC cholinesterase activities were inhibited in males by 24% and 40%, respectively, and in females, by 38 and 39%, respectively. For the subchronic neurotoxicity study, the LOAEL for systemic toxicity was established at 1486 and 1575 mg/kg/day in males and females, respectively, based on decreased body weight and food consumption, anogenital staining, and red nasal staining; the NOAEL for systemic toxicity was established at 352 and 395 mg/kg/day for males and females, respectively. The LOAEL for ChEI was established at 352 and 395 mg/kg/day in males and females, respectively, based on plasma (12-20%, males; 15-30%, females) and RBC (49-61%, males; 49-53%, females) ChEI in males and females and brain (cortex) ChEI in females (12-20%); the NOAEL is 4 mg/kg/day.

Table 7. Summary of Neurotoxicity Study Data for Malathion.

Guideline	Study Type (Test Material)	MRID (Date)	Results
870.6100 (81-7)	Acute Oral Delayed Neurotoxicity in the Hen **(Malathion technical 93.6%)**	40939301 (1988)	Neither gross necropsies nor histopathological examination revealed any treatment-related effects in treated hens. Negative for any evidence of acute delayed neurotoxicity.
870.6200 (81-8)	Acute oral neurotoxicity in the Rat **(Malathion technical 96.4%)**	43146701 (1994)	NOAEL = 1000 mg/kg LOAEL = 2000 mg/kg (limit dose), based on decreased motor activity and clinical signs at the peak time of effect on day 1 (15 min post dosing) and plasma and RBC ChEI at day 7.
870.6200 [82-5(b)]	Subchronic Neurotoxicity Study in the rat **Malathion technical (96.4%)**	43269501	NOAEL (M/F): 4 mg/kg/day LOAEL (M/F): 352/395 mg/kg/day, based on plasma, RBC ChEI in males and females and brain ChEI in females. No neurotoxicity noted at high-dose.

3.2.8 Metabolism Studies

[^{14}C]Malathion was administered as a single oral gavage dose to groups of 5 male and 5 female Sprague-Dawley rats at 40 mg/kg (low dose), at 800 mg/kg (high dose) or at 40 mg/kg (following 15 days of dosing with non-radiolabeled material). Radioactivity in urine and feces was determined at 4, 8, 12, 24, 48, and 72 hours after dosing. At 72 hours, animals were sacrificed and major organs/tissues were analyzed for radioactivity. Individual and pooled urine and fecal samples were analyzed for biotransformation products at 0-24 and 24-48 hours after dosing.

In the rat, malathion is excreted primarily in the urine (80-90%) in the first 24 hours following exposure, with lesser amounts excreted in the feces. At 72 hours, the highest concentration of radioactivity was observed in the liver, but less than 0.3% of the administered radioactivity was present in that organ. Radioactivity did not bioaccumulate in any of the organ/tissues analyzed. Although eight radiolabeled metabolites were observed in urine, greater than 80% of the radioactivity in urine was represented by the diacid (DCA) and monoacid (MCA) metabolites. The remaining radiolabeled metabolites were identified as components of "peak A" and "peak B". It was determined that between 4 and 6% of the administered dose was converted to malaoxon, the active cholinesterase inhibiting metabolite of malathion.

Table 8. Metabolism of Malathion in Spraque-Dawley Rats.

Guideline	Study Type (Test Material)	MRID (Date)	RESULTS
870.7485 85-1	General Metabolism-Rat	41367701 (1989)	Malathion is excreted primarily in the urine (80-90%) in the first 24 hours following exposure, with lesser amounts excreted in the feces. At 72 hours, the highest concentration of radioactivity was observed in the liver, but less than 0.3% of the administered radioactivity was present in that organ. Radioactivity did not bioaccumulate in any of the organ/tissues analyzed. Although eight radiolabeled metabolites were observed in urine, greater than 80% of the radioactivity in urine was represented by the diacid (DCA) and monoacid (MCA) metabolites. The remaining radiolabeled metabolites were identified as components of "peak A" and "peak B". It was determined that between 4 and 6% of the administered dose was converted to malaoxon, the active cholinesterase inhibiting metabolite of malathion.

3.2.9 Dermal Absorption

No guideline dermal penetration study has been submitted to the Agency in support of reregistration. HED's HIARC concluded that a dermal absorption factor of 10% should be used for converting oral dosing to dermal dosing. This conclusion is based in part on published literature data. In a study with human volunteers (Feldman, R.J. and Maibach, H.I., 1970), [14C]malathion was applied to unprotected skin on the ventral surface of the forearms of 7 subjects. Urine was collected for 5 days and assayed for total radioactivity. A mean of 7.85% ± 2.71% of the applied radioactivity was recovered in the 5 day urine, indicating a dermal absorption rate of approximately 5 to 10% over a 5 day period. The 10% dermal absorption factor is supported by comparison of NOAELs and LOAELs in the oral developmental toxicity study and the 21-day dermal toxicity study in the same species (rabbits).

3.3 FQPA Considerations

In HED's FQPA Safety Factor Recommendations (Combined Report of the HIARC and Safety Factor Committee and its Recommendation for the Organophosphates), dated August 6, 1998, it was concluded that the FQPA Safety Factor (as required by the Food Quality Protection Act of August 3, 1996) be **removed** in assessing the risk posed by this chemical. This conclusion was based on the following factors: (i) developmental toxicity studies showed no increased sensitivity in fetuses as compared to maternal animals following *in utero* exposures in rats and rabbits; (ii) a two-generation reproduction toxicity study in rats showed no increased sensitivity in pups when comparted to adults; and (iii) the toxicology data base is complete and there are no significant data gaps at this time.

3.4 Endpoint Selection

HED's Hazard Identification Assessment Review Committee (HIARC) reviewed the toxicological database for malathion and selected toxicological endpoints for acute and chronic dietary and for occupational (dermal and inhalation) exposure risk assessment on November 6, 1997 (memorandum dated December 17,1997). Following that meeting, the Agency pursued the external review mechanism to address a number of additional issues. The external peer review panel's comments were evaluated in HIARC meetings on August 18, 20 and 27, 1998 and are documented in the HIARC's report, "Malathion Re-evaluation" dated December 22, 1998. The doses and toxicological endpoints selected for various exposure scenarios are summarized in Table 9.

A common toxicological endpoint exists (cholinesterase inhibition) for the dermal and inhalation routes. However, because the uncertainty factors are dissimilar (i.e., 100 for the dermal route, and 1000 for the inhalation route), MOEs should be combined using the aggregate risk index (ARI) method to estimate combined risk from dermal and inhalation routes.

Table 9. Summary of Doses and Endpoints Selected for Malathion Risk Assessments.

EXPOSURE SCENARIO	DOSE (mg/kg/day)	ENDPOINT	STUDY
Acute Dietary (single day)	NOAEL=50	Maternal toxicity	Range Finding and Main Developmental Toxicity Studies - Rabbits
	UF=100 (10X10)	**Acute RfD = 0.5 mg/kg/day**	
	FQPA Safety Factor Removed (1x)	**Acute PAD = 0.5 mg/kg/day**	
Chronic Dietary	NOAEL=2.4	Inhibition of plasma cholinesterase activity	Combined Chronic Toxicity/ Carcinogenicity Study in the Rat
	UF=100 (10X10)	**Chronic RfD = 0.024 mg/kg/day**	
	FQPA Safety Factor Removed (1x)	**Chronic PAD = 0.024mg/kg/day**	
Carcinogenicity	The cancer risk estimate is calculated using a linear Q1* of 1.52×10^{-3} $(mg/kg/day)^{-1}$ based on combined liver adenomas and/or carcinomas in female rats.		
Short-Term (Dermal) 1-7 days	NOAEL=50	Inhibition of plasma, RBC, and brain cholinesterase activity	21-day Dermal Study in the Rabbit
	UF=100 (10X10) for occupational and non-occupational populations (FQPA Safety Factor Removed (1x)		
Intermediate-term (Dermal) 1 week to several months	NOAEL = 50	Inhibition of plasma, RBC, and brain cholinesterase activity	21-day Dermal Study in the Rabbit
	UF=100 (10X10) for occupational and non-occupational populations (FQPA Safety Factor Removed (1x))		
Long-Term (Dermal) >180 days	Oral NOAEL = 2	Inhibition of plasma cholinesterase activity	Combined Chronic Toxicity/ Carcinogenicity Study in the Rat
	UF=100 (10X10) for occupational and non-occupational populations (FQPA Safety Factor Removed (1x)) dermal absorption = 10%		
Inhalation (Short, Intermediate, and Long Term)	LOAEL = 25.8 mg/kg/day The inhalation LOAEL of 0.1 mg/L was converted to 25.8 mg/kg/day.	Inhibition of plasma and RBC cholinesterase activity and histopathology in respiratory epithelium	90-Day Inhalation Study in the Rat
	UF = 1000 10x10x10 for the lack of a NOAEL and the severity of the nasal lesions observed in the two-week range finding study (100% inhalation absorption) for all occupational and non-occupational populations which include infants and children (FQPA Safety Factor Removed (1x)).		

The inhalation LOAEL of 0.1 mg/L was converted to an oral equivalent dose of 25.8 mg/kg/day for use in MOE calculations based on HED's route-to-route extrapolation methodology (J. Whalen and H. Pettigrew, October 10, 1998).

3.5 Endocrine Disrupter Effects

The Food Quality Protection Act (FQPA; 1996) requires that EPA develop a screening program to determine whether certain substances (including all pesticides and inerts) "may have an effect in humans that is similar to an effect produced by a naturally occurring estrogen, or such other endocrine effect...." EPA has been working with interested stakeholders, including other government agencies, public interest groups, industry and research scientists to develop a screening and testing program as well as a priority setting scheme to implement this program. The Agency's proposed Endocrine Disrupter Screening Program was published in the Federal Register of December 28, 1998 (63 FR71541). The Program uses a tiered approach and anticipates issuing a Priority List of chemicals and mixtures for Tier 1 screening in the year 2000. As the Agency proceeds with implementation of this program, further testing of malathion and end-use products for endocrine effects may be required.

4.0 EXPOSURE ASSESSMENT

4.1 Summary of Registered Uses

Malathion is a non-systemic, wide spectrum organophosphorus insecticide. It is used in the agricultural production of a wide variety of terrestrial food and feed crops to control insects such as aphids, leafhoppers, and Japanese beetles. Malathion is also used in mushroom houses, in grain storage facilities, agricultural premises (outdoor bait), and as a general wide-area treatment for mosquito-borne disease control. Malathion is available to the home gardener for outdoor residential uses which include vegetable gardens, home orchards, ornamentals and lawns.

Malathion is formulated as an emulsifiable concentrate (EC), a dust (D), a wettable powder (WP), a ready-to-use (RTU), and as a pressurized liquid (PrL). The EC and RTU formulations may contain up to 82% and 95% ai, respectively. Several of the 95% ai liquids are intended for ultra-low-volume (ULV) application using aerial or ground equipment. Malathion is typically applied as multiple foliar treatments as needed to control the pest species.

There are 254 end-use products currently listed in OPP's REFS database (search conducted May 17, 1999) as active product registrations. Many of these products list use sites not supported by the basic producer (Cheminova Agro A/S). The Agency has been informed by the basic producer (Cheminova) and IR4 that the following use sites will not be supported for reregistration:

All pet uses for all formulations;
All livestock uses with all formulations;
All indoor uses (except stored commodities and storage facilities);
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)
- Peavines (including hay)
- Safflower seed
- Soybeans (including hay and forage)
- Sugar beets
- Sunflower seed
- Treated raisin trays

All pressurized can formulations.

Consequently, most of these use sites, while they may be included in the list of currently registered uses, have not been specifically included in the exposure/risk assessment in this document.

Table 10. Summary of Use Patterns for Malathion

Market Segment	Use Sites	Formulation	Application Method	Application Rate	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 ai/acre	First year: 6-8 applications, every 7-10 days Second year: only as pest insult indicates
	Medfly Control (Section 18)	EC (ULV) mixed with protein bait as spray	Aerial Ground (backpack and truck-mounted mist blowers)	0.175 lb ai/acre	Application frequency and intervals between application are based on pest pressures specific to the Section 18 exemption.
General Agriculture	Food/Feed[1] * Alfalfa * Cotton * Rice * Sorghum * Wheat	EC (including ULV) WP Dusts	Aerial Groundboom Airblast Power Duster	0.15 to 6.0 lb ai/acre	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
	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	2.6 to 8.7 lb ai/acre	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 lb ai/acre	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	0.0003 to 0.000085 lb ai/sq ft	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.

4.2 Dietary Exposure

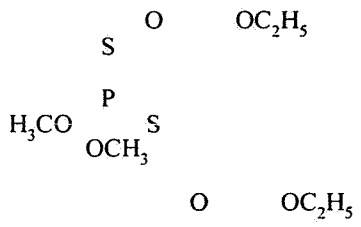
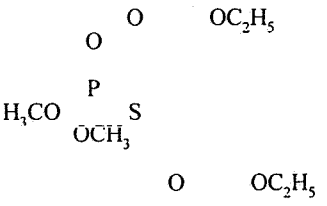
Potential exposure to residues of malathion and its malaoxon metabolite in the diet occurs through food and water sources. Malathion is typically applied to crops multiple times during the growing season. It is also applied postharvest directly to cereal grains in storage silos. The field trial residue data supporting reassessed tolerances indicate there are quantifiable residues of malathion on edible crops; however, there is little (if any) likelihood of residue transfer to meat and milk. Field trial and metabolism data indicate that malaoxon is usually a minor metabolite in plants, if detected at all. Based on laboratory studies, malathion is not likely to persist in surface water or expected to leach to ground water. Screening-level model estimates indicate the contribution of malathion residues to dietary exposure through drinking water does not result in an aggregate (food + water) exposure concern.

4.2.1 Dietary Exposure (food source)

Tolerances have been established for residues of malathion *per se* in/on food/feed commodities [40 CFR §180.111, §185.3850, §185.7000, and §186.3850] and meat, milk poultry and eggs [40 CFR §180.111]. Because animal metabolism data indicate that there is little likelihood of residue transfer to meat, milk, poultry and eggs, tolerances for malathion residues in these commodities may be revoked. Based on available plant metabolism data, the HED Metabolism Committee has determined that the malathion residues of concern in plants consists of malathion and its metabolite malaoxon; see Figure A for chemical structures and full chemical names. The tolerance expression (currently expressed in terms of malathion *per se*) should be revised to include malathion and malaoxon.

The Codex Alimentarius Commission has established several maximum residue limits (MRLs) for residues of malathion in/on various raw agricultural and processed commodities. The Codex MRLs are expressed in terms of malathion *per se*. The Codex MRLs and the U.S. tolerances will be incompatible when the U.S. tolerance expression for plant commodities is revised to include both residues of malathion and the metabolite malaoxon

Figure A. Chemical Names and Structures of Malathion Residues of Concern in Plant Commodities.

Common Name Chemical Name	Chemical Structure	**Common Name** Chemical Name	Chemical Structure
Malathion		**Malaoxon; Maloxon; Malathion Oxygen Analog**	
O,O-dimethyl dithiophosphate of diethyl mercaptosuccinate		*O,O*-dimethyl thiophosphate of diethyl mercaptosuccinate	

24
25

Metabolism studies with alfalfa, lettuce, cotton, and wheat adequately depict the qualitative nature of the residue in plants. The metabolic pathway for malathion in these plants is similar: oxidation of malathion to malaoxon and de-esterification to form mono- and dicarboxylic acids and succinate derivatives. Residues were predominately found in edible vegetative portions and were also present in cotton seed and wheat grain following foliar application. Unchanged malathion was typically found to be the major residue; malaoxon, when present, comprised a very small portion ($\leq$1%) of the total radioactivity.

The submitted residue data from field trials and processing studies depict combined residues of malathion and its malaoxon metabolite. Combined residues of malathion and its malaoxon metabolite are likely to be found at detectable levels in samples of raw and processed commodities following preharvest and postharvest applications; however, malaoxon is usually a minor metabolite, if detected at all. In general, field trials met the criteria for the required number of samples and were conducted in locations representative of the major growing regions specific to the crop tested. The test systems utilized representative product formulations, applied at maximum rates using application equipment in accordance with label specifications. These data were obtained using analytical methods adequately validated for data collection. Storage stability data support the integrity of the residue data for malathion and malaoxon. For the determination of malathion and malaoxon residues in plant commodities, the registrant has proposed flame photometric detection (FPD) method M-1866 as an enforcement method. The limit of quantification (LOQ) of each compound is 0.05 ppm. Method M-1866 has undergone a successful independent laboratory validation, and acceptable radiovalidation data using samples from an alfalfa metabolism study have also been submitted and evaluated. Pending a successful tolerance method validation to be conducted by EPA's Analytical Chemistry Laboratory, Method M-1866 will be approved for enforcement purposes.

Ruminant and poultry metabolism studies have been submitted, evaluated, and found acceptable to fulfill animal metabolism reregistration requirements. Neither malathion nor malaoxon were observed in eggs, milk, and animal tissues following oral administration of [^{14}C]malathion at exaggerated rates. The residues of malathion in animal commodities represent a Category 3 situation under 40 CFR §180.6(a): i.e., situations in which it is not possible to establish with certainty whether finite residues will be incurred under reasonable worst case exposure scenarios, but there is no reasonable expectation of the occurrence of finite residues in animal commodities. Therefore, there is no need for tolerances in these commodities based on livestock dietary exposure to malathion.

The current malathion tolerances for animal commodities were established based on use patterns involving direct animal treatments which would, in all probability, result in significant malathion residues of concern in eggs, milk, and animal tissues. Therefore, if the direct animal treatment uses of malathion to poultry and livestock animals are canceled, then the established tolerances for residues of malathion *per se* in eggs, milk, and animal tissues may be revoked (Greybeard Committee decision on Malathion, 10/19/94). Note: The registrant has indicated they do not intent to support direct livestock treatment for reregistration. If another party wished to do so, then appropriate dermal metabolism and magnitude of the residue studies are required. For the determination of residues of malathion *per se* in animal commodities, the Pesticide Analytical Manual (PAM, Vol. II, §180.111) lists GLC Methods A and B for enforcement of malathion tolerances.

Residue data from crop field trials, processing studies, and livestock feeding studies have been reviewed for the purpose of tolerance reassessment. HED has high confidence in the available, geographically representative, field trial data. HED is recommending revocation of tolerances for certain commodities for one or more of the following reasons: (1) established tolerances for animal commodities may be revoked if direct animal treatment uses are canceled; (2) there are no longer significant livestock feed items for the commodity; and (3) currently there are no registered uses.

Insufficient field trial data are available to reassess the tolerances for apples, dates, quinces, sorghum (forage), and vegetables (leafy except Brassica). Existing tolerances for these commodities have been used for dietary exposure estimates.

4.2.2 Dietary Exposure Characterization

The acute and chronic dietary exposure assessments were conducted using the Dietary Exposure and Evaluation Model (DEEM™) system. DEEM can be used to estimate exposure to constituents in foods comprising the diets of the U.S. population, including population subgroups. The software contains food consumption data from the USDA Continuing Survey of Food Intake by Individuals (CFSII) from 1989-1992. For the chronic exposure assessment, consumption data are averaged for the entire U.S. population, and within population subgroups such as "all infants". For acute dietary exposure estimates, the program references each individual day of recorded consumption and produces a distribution of daily exposures for individuals comprising the U.S. population and population subgroups. In the case of malathion, the dietary exposure distribution based on point estimates for residues in foods was used to estimate an upper-bound for acute risk (e.g., a deterministic approach).

Residue inputs to the malathion DEEM analysis included anticipated residues (W. Smith, May 19, 1999). The acute residues are based on reassessed tolerances. The chronic anticipated residues are also based on reassessed tolerances and residue data from available crop field trials, PDP/USDA FDA monitoring data, and weighted average percent crop treated data (G. Ali; November, 1997).

The Reference Dose (RfD) is derived from an exposure level at which there are no statistically or biologically significant increases in the frequency or severity of adverse effects between the exposed population and its appropriate control, along with the application of uncertainty factors. The percent of the RfD is calculated as the ratio of the exposure value to the RfD (exposure/RfD x 100 = % RfD). The population adjusted dose (PAD) is an adjusted RfD reflecting the retention or reduction of the FQPA safety factor for all populations which include infants and children. For malathion, the acute population adjusted dose (aPAD) and chronic population adjusted dose (cPAD) is 0.5 mg/kg/day and 0.024 mg/kg/day, respectively.

The following equations are used to express dietary exposure and risk:

$$\text{Dietary Exposure (mg/kg/day)} = (\text{consumption} \times \text{residue})$$

$$\text{Dietary Risk (\%PAD)} = \frac{\text{Dietary Exposure (mg/kg/day)}}{\text{Population Adjusted Dose (mg/kg/day)}}$$

4.2.2.1 Acute Dietary Exposure

It should be noted that cholinesterase inhibition is not the adverse effect of concern for acute dietary exposure to malathion. When the cumulative exposure assessment for organophosphorous chemicals is conducted, the acute dietary pathway for malathion will be evaluated to determine whether it should be included or excluded from the quantitative cumulative exposure assessment. Thus, the acute dietary assessment was not refined for purposes of completing the acute aggregate risk assessment for malathion.

For the Tier 1 acute dietary analysis of malathion, exposure (consumption x residue) was compared to an acute population adjusted dose of 0.5 mg/kg/day. The acute dietary risk analysis estimates the distribution of single day exposures for the overall U.S. population and certain subgroups. The analysis evaluates exposure to the chemical for each food commodity and assumes uniform distribution of

malathion in the food supply. The Tier 1 DEEM analysis at the 95% exposure percentile is based on reassessed tolerance level residues. Only the crops supported for reregistration were included and all meat, milk, poultry and egg tolerances were omitted. Reduction factors for grape juice, citrus juice, apple juice, raisins, tomato puree, tomato catsup, milled rice, corn oil, cottonseed oil, and cottonseed meal were used rather the default concentration factors. The concentration factor for mint oil was not used.

As shown in Table 11, the acute dietary residue contribution at the 95th exposure percentile occupied less than 100% of the aPAD for any population subgroup and therefore does not exceed HED's level of concern. For the most highly exposed subgroup, children 1-6, residue contribution occupied 38% of the aPAD. HED refers to the 95th percentile of exposure for risk assessments based on use of upper-end residues (tolerances) in a deterministic-type risk assessment. This Tier 1 acute analysis for malathion is an upper-bound estimate with all input residues equal to the reassessed tolerance value and the assumption that 100% of the crop is treated nationwide.

Table 11. Summary of Tier 1 Acute Dietary Exposure Analysis for Malathion.

Population Subgroup	95th Percentile of Exposure	
	Exposure (mg/kg/day)	%aPAD[a]
U.S. Population	0.100107	20
Non-nursing Infants <1 year	0.177455	35
Children 1-6	0.190584	38
Children 7-12	0.126309	25
Females 13-50	0.065749	13
Males 13-19	0.082187	16
Males 20+	0.069027	14

4.2.2.2 Chronic Dietary Exposure

A chronic exposure analysis was conducted using the DEEM ™ exposure software. The input values for the Tier 3 analysis include highly refined anticipated residues derived from USDA/PDP and FDA monitoring data, reassessed tolerances, average field trial data, processing studies and percent crop treated information from BEAD (G. Ali; November, 1997). Exposure (consumption x residue) was compared to the chronic population adjusted dose of 0.024 mg/kg/day.

The field trial and processing data used in deriving these anticipated residues include malathion and malaoxon. Monitoring data on malathion and malaoxon are reported separately by FDA and not all analytical methods used are capable of detecting both. PDP reports residues only for malathion. Therefore, the monitoring data represent malathion only. Nevertheless, in our judgement, the potential level of malaoxon residues in the samples monitored is adequately covered. Between 1992 and 1996 the FDA monitored 37,492 food samples for the oxygen analog of malathion with only four positive samples. Three samples of bread imported from Russia had low levels of malaoxon and one sweet pea sample from the United States had a positive detection. Field trial and metabolism studies also indicate

that malaoxon is usually a minor metabolite, if detected at all. Two approaches to estimating the non-detectable malaoxon residues in the monitoring data were considered. One was to assume that malaoxon was present in all malathion samples at a level of ½ the limit of detection (LOD). The other procedure was to assume that malaoxon was not detectable in all samples and use a more conservative estimate of malathion residues in those samples for which it was nondetectable, i.e., use ½ the limit of quantitation(LOQ), with the assumption that the overestimate of residues (the LOQ is generally over 3 times higher than the LOD) would cover any trace levels of malaoxon that could be present in some of the samples. The second approach was adopted in this assessment.

Residues are not expected to be present in livestock commodities; thus, meat and milk food forms were not included in the dietary exposure analysis. Although PDP and FDA monitoring data for malathion in milk are available, these data were not used in the dietary exposure analysis because residues of malathion and malaoxon are not expected to be present in livestock commodities. The PDP data sets contain about 1300 samples collected in 1996-1997 with no detectable residues at 0.001 to 0.002 LODs. The FDA data sets contain many samples of milk, butter, cheese, etc. over the years with no detections of malathion or malaoxon.

As shown in Table 13, the chronic dietary residue contribution occupies less than 100% of the cPAD for all population subgroups and therefore does not exceed HED's level of concern. For the most highly exposed subgroup, children 1-6, the residue contribution occupies 4% of the cPAD.

Table 13. Summary of Tier 3 Malathion Chronic Dietary Exposure Analysis by DEEM.

Population Subgroup	Exposure (mg/kg bw/day)	Percent of Chronic PAD [a]
U.S. Population	0.000386	2
All Infants <1 year	0.000643	3
Non-nursing Infants	0.000832	4
Children 1-6	0.000845	4
Children 7-12	0.000625	3
Females 13-50	0.000295	1
Males 13-19	0.000426	2
Males 20+	0.000307	1

4.2.2.3 Carcinogenic Risk

Carcinogenic risk for malathion in the food supply is below HED's level of concern. Carcinogenic risk for malathion is quantified, based on the estimated average dietary exposure of the General U.S. population (0.000386 mg/kg bw/day) multiplied by the *upper-bound* potency factor (Q_1^*) of 1.5×10^{-3} $(mg/kg\ bw/day)^{-1}$. On this basis, the upper-bound carcinogenic risk estimate for malathion is calculated to be 5.8×10^{-7}. Generally, risks greater than the 1×10^{-6} range are considered of risk concern by the Agency.

4.2.3 Dietary Exposure (drinking water source):

The Environmental Fate and Effects Division (EFED; Birchfield and Birchfield, et al.) provided an analysis of available monitoring data and a screening-level assessment using simulation models to estimate the potential concentration of malathion and its degradate malaoxon in ground and surface water. The fate data on malathion indicate that it is extremely mobile and shows little persistence in soil and water. The primary route of dissipation of malathion in surface soils appears to be aerobic metabolism. Limited fate data are available for the degradate malaoxon. However, based on its chemical similarity to malathion, the parent and its degradate are expected to have similar chemical properties. Malathion and its degradates in general are soluble and do not adsorb strongly to soils.

Surface Water Modeling: The GENEEC model predicts that combined malathion and malaoxon surface water peak concentration of **322 μg/L** and a 56-day average concentration of **97 μg/L**. These values represent upper-bound estimates of the concentrations that might be found in surface water based on simulations performed using a maximum application rate of 6.25 lb ai/A applied 1-25 times with a 3-30 day interval between applications. The model input for aerobic soil metabolism half-life was 3 days for malathion and 21 days for malaoxon. Malaoxon levels were estimated with the GENEEC model with the assumption that fate variables, which were not known, were the same as malathion. The PRZM-EXAMs model predicts a multi-year mean malathion *per se* concentration of **4 μg/L.**

Ground Water Monitoring/Modeling: First tier groundwater concentrations were derived from monitoring data because they were higher than results predicted using the SCI-GROW model. The highest detected malathion concentration in groundwater was **3 μg/L**. Malaoxon was not examined in this study but the same value is expected to be a conservative estimate of malaoxon concentration. Therefore, EFED recommended conservative ground water estimates of **3 μg/L** for malathion and **3 μg/L** for malaoxon based on the assumption that the concentration of malaoxon will not exceed malathion.

The estimated environmental concentration (EEC) of malathion and malaoxon were compared to drinking water levels of comparison (DWLOCs). The DWLOC is a theoretical upper limit of a pesticide's concentration in drinking water in light of total aggregate exposure to a pesticide in food, drinking water, and through residential uses. OPP uses DWLOCs internally in the risk assessment process as a surrogate measure of potential exposure associated with pesticide exposure through drinking water. DWLOC values are not regulatory standards for drinking water. They do have an indirect regulatory impact through aggregate exposure and risk assessments. Three DWLOC assessments were conducted: acute which utilized the **322 μg/L** value, chronic which utilized a **32 μg/L** value (97 μg/L divided by a factor of **3 = 32 μg/L**), and cancer which utilized the **4 μg/L** value.

4.2.3.1 DWLOCs for Chronic (Non-Cancer) Exposure

Chronic DWLOCs were calculated based on the chronic dietary (food) exposure and standard body weights and water consumption figures. The Agency's standard body weights and water consumption values used to calculate DWLOCs are as follows: 70kg/2L (adult male), 60 kg/2L (adult female), and 10 kg/L (child). To calculate the DWLOC, the chronic dietary food exposure was subtracted from the chronic PAD using the equation

$$DWLOC_{chronic} = \frac{[\text{chronic water exposure (mg/kg/day)} \times \text{(body weight)}]}{[\text{consumption (L)} \times 10^{-3}\ \text{mg}/\mu\text{g}]}$$

where chronic water exposure (mg/kg/day) = [cPAD - (chronic food (mg/kg/day)]

As shown in Table 14, the drinking water estimated concentrations in ground water (6 μg/L) and surface water (32 μg/L) are all below HED's DWLOCs for malathion for all population subgroups. Based on the available information, residues of malathion in drinking water do not result in an unacceptable contribution to chronic dietary exposure at this time.

Table 14. Drinking Water Levels of Comparison for Chronic Dietary Exposure.

Population Subgroup	Chronic PAD (mg/kg/day)	Food Exposure (mg/kg/day)	Max. Water Exposure (mg/kg/day)	$DWLOC_{chronic}$ (μg/L)	GENEEC[a] (μg/L)	Ground Water Monitoring (μg/L)[b]
U.S. Population	0.024	0.000386	0.02361	413	32	6
Females (13-19)	0.024	0.000371	0.02363	354	32	6
Infants <1 yr	0.024	0.000832	0.02317	232	32	6
Children 1-6	0.024	0.000845	0.02316	232	32	6

[a] Includes malathion at 21 μg/L and malaoxon at 75 μg/L (96 ÷ 3 = 32 μg/L)
[b] Includes malathion at 3 μg/L and malaoxon at an equal concentration of 3 μg/L.

4.2.3.2 DWLOCs for Acute Exposure

Acute DWLOCs were calculated based on the acute dietary (food) exposure and standard body weights and water consumption figures. The Agency's standard body weights and water consumption values used to calculate DWLOCs are as follows: 70kg/2L (adult male), 60 kg/2L (adult female), and 10 kg/L (child). To calculate the acute DWLOC, the acute dietary food exposure was subtracted from the acute PAD using the equation

$$DWLOC_{acute} = \frac{[\text{acute water exposure (mg/kg/day)} \times \text{(body weight)}]}{[\text{consumption (L)} \times 10^{-3}\ \text{mg}/\mu\text{g}]}$$

where acute water exposure (mg/kg/day) = [aPAD - acute food (mg/kg/day)].

As shown in Table 15, acute the drinking water estimated concentrations in ground water (6 μg/L) and surface water (322 μg/L) are below HED's DWLOCs for malathion. HED concludes that based on the available information, modeled residues in drinking water do not indicate an unacceptable contribution to acute dietary exposure at this time.

Table 15. Drinking Water Levels of Comparison for Acute Dietary Exposure.

Population Subgroup	Acute PAD	Food Exposure (mg/kg/day)	Water Exposure (mg/kg/day)	$DWLOC_{acute}$ (μg/L)	GENEEC (μg/L)[a]	Ground Water Monitoring (μg/L)[b]
U.S. Population	0.5	0.100107	0.399893	13996	322	6
Females (13-50)	0.5	0.065749	0.434251	13028	322	6
Infants <1 yr	0.5	0.177455	0.322545	3225	322	6
Children 1-6	0.5	0.190584	0.309416	3094	322	6

[a] Includes malathion at 226 μg/L and malaoxon at 96 μg/L.
[b] Includes malathion at 3 μg/L and malaoxon at an equal concentration of 3 μg/L.

4.2.3.3 DWLOCs for Cancer

DWLOCs for cancer, excluding the contribution from residential exposure, are calculated based on chronic dietary (food) exposure and standard body weights and water consumption figures. The Agency's standard body weights and water consumption values used to calculate DWLOCs are as follows: 70kg/2L (adult male) and 60 kg/2L (adult female). To calculate the DWLOC for cancer, the chronic dietary food exposure was subtracted from the negligible risk divided by the Q_1* using the equation:

$$DWLOC_{cancer} = \frac{[\text{cancer water exposure (mg/kg/day) x (body weight)}]}{[\text{consumption (L) x } 10^{-3} \text{ mg}/\mu\text{g}]}$$

$$\text{Where Cancer } H_2O \text{ Exposure (mg/kg/day)} = \frac{\text{Negligible risk}}{Q_1^*} - [\text{chronic food}]$$

As shown in Table 16, the drinking water estimated concentrations in ground water (3 μg/L) and surface water (4 μg/L) are less than HED's DWLOCs for malathion. HED concludes that based on the available information, modeled residues in drinking water do not indicate an unacceptable contribution to dietary exposure for cancer risks at this time. Note that these calculations do not include the contribution from residential dermal and inhalation exposure because exposure from these sources alone are of risk concern.

Table 16. Summary of DWLOC calculations for cancer - Dietary Contribution Only.

Population	Negligible Risk	Q* $(mg/kg/day)^{-1}$	Chronic Food Exposure (mg/kg/day)	Chronic H_2O Exposure (mg/kg/day)	$DWLOC_{cancer}$ (μg/L)	PRZM-EXAMS (μg/L)[a]	Ground Water Monitoring (μg/L)[b]
Adult Male	1.00e-06	1.52e-03	0.000386	0.00027	10	4	6
Adult Female	1.00e-06	1.52e-03	0.000295	0.00036	11	4	6

[a] Includes malathion parent only.
[b] Includes malathion at 3 μg/L and malaoxon at an equal concentration of 3 μg/L.

4.4 Non-Dietary Exposure

Malathion is widely used in agricultural, commercial, and residential settings. It is also used as a general wide-area treatment for mosquito-borne disease control. Occupational and non-occupational (residential) exposure to malathion and malaoxon residues via dermal and inhalation routes can occur during handling, mixing, loading, and applying activities. Postapplication exposure potentials also exist. There is potential dermal exposure to persons entering treated sites (occupational and non-occupational) following application of malathion-containing products. There is also potential for dermal and inhalation exposure to individuals (bystanders) contacting lawns at home or in public areas from aerial or ground applications for mosquito control. In regard to the potential for residential exposure and risk from spray drift associated with the agricultural use of malathion, the potential for spray drift associated with ground and aerial application for mosquito control is believed to represent a worse case exposure as compared to residential exposure adjacent to agricultural areas.

Based on toxicological criteria and potential for exposure, HED has conducted dermal and inhalation exposure assessments for the occupational handler and postapplication dermal exposure assessments for occupational workers. HED has also conducted dermal exposure assessments for the residential handler and postapplication dermal and inadvertent oral ingestion exposure to adults and/or children.

4.4.1 Occupational Handler Exposure Scenarios

HED has identified 16 major exposure scenarios for which there is potential for occupational handler exposure during mixing, loading, and applying products containing malathion to agricultural crops and to non-agricultural use sites. These occupational scenarios reflect a broad range of application equipment, application methods, and use sites. The scenarios were classified as short-term (1-7 days) and intermediate-term (1 week to several months) based primarily on the frequency of exposure. A long term exposure duration (i.e., continuous exposure of $\geq$ 180 days) is not expected because malathion use is seasonal and intermittent. Most commercial applicators are not expected to be employing malathion exclusively in insect management programs.

The estimated exposures considered baseline protection (long pants and a long-sleeved shirt, no gloves, and an open cab or tractor), additional personal protective equipment (PPE, which includes a double layer of clothing and gloves and/or a dust/mist respirator), and engineering controls (closed mixing/loading systems for liquids and wettable powders and enclosed cabs/trucks).

4.4.1.1 Occupational Handler Exposure Data Sources and Assumptions

Chemical specific data for assessing human exposures during pesticide handling activities were not submitted to the Agency in support of the reregistration of malathion. It is the policy of HED to use data from the Pesticide Handlers Exposure Database (PHED) Version 1.1 to assess handler exposures for regulatory actions when chemical-specific monitoring data are not available. While data from PHED provide the best available information on handler exposure, it should be noted that some aspects of the study data (e.g., duration, acres treated, lb of active ingredient handled) may not accurately represent labeled uses in all cases. HED has developed a series of tables of standard unit exposure values for many occupational scenarios that are utilized to ensure consistency in exposure assessments.

The following assumptions and factors were used to complete this exposure assessment:

- Average body weight of an adult handler is 70 kg. This body weight is used in both the short- and intermediate-term assessment, since the endpoint of concern is not sex-specific (i.e., the

cholinesterase inhibition could be assumed to occur in males or females).

- Average work day interval represents an 8 hour workday (e.g., the acres treated or volume of spray solution prepared in a typical day).

- Daily acres and volumes (as appropriate) to be treated in each scenario include:

  - 350 acres for aerial and chemigation applications (including flaggers supporting aerial applications);
  - 1,500 acres for mosquito aerial applications (including flaggers and non-ULV, e.g., EPA Reg. Nos. 10827-38 & 5905-196);
  - 800 acres for ULV aerial applications to agricultural crops;
  - 7,500 acres for ULV aerial applications to mosquitoes (including flaggers, although the use of flaggers may be unlikely for this scenario);
  - 80 acres for groundboom applications to agricultural crops and berries;
  - 10 acres for groundboom applications to ornamentals;
  - 40 acres for airblast applications on agricultural crops, berries, and ornamentals;
  - 160 gallons for fogger applications on mosquitoes using a thermal fogger;
  - 16 gallons for ULV fogger applications on mosquitoes using a non-thermal fogger;
  - 6,000 square feet for power duster to grain stored in storage silos;
  - 40 gallons for a low pressure handwand to treat stored grain facilities and agricultural premises;
  - 1000 square feet for low pressure handwand spot treatment of turf;
  - 5 acres for a low pressure handwand to ornamentals;
  - 5 acres for handgun turf;
  - 9,000 square feet for a hose end sprayer to mushroom houses;
  - 5 gallons for a paintbrush to windows screens and wineries for pest control.

- For fogging mosquitoes with a fogger, no PHED data were available; thus, as a surrogate, the PHED baseline unit exposure data for an airblast sprayer (0.36 mg/lb ai for dermal and 4.5 µg/lb for inhalation) were used to calculate dermal and inhalation exposure. In addition, the gallons handled were taken from information provided on the label (EPA Reg. No. 4787-8) which indicated that a thermal fogger sprays at a rate of 40 gal/hr and a non-thermal fogger sprays at a rate of 4 gal/hr. EPA assumed the fogger was used 4 hrs per day.

- For loading dusts for a power duster, no PHED data were available; thus, as a surrogate, the PHED baseline unit exposure data for wettable powders (3.7 mg/lb ai for dermal and 43 µg/lb for inhalation) were used to calculate dermal and inhalation exposure.

- Calculations are completed for a range of maximum application rates from residue field trials in support of food tolerance for agricultural uses. For non-agricultural uses maximum application rates were identified for crop groupings, as listed on the available malathion labels and LUIS reports. This results in an exposure/risk assessment that brackets risk levels associated with the various use patterns.

- When scenario-specific data are not available, HED calculates unit exposure values using generic protection factors that are applied to represent the use of personal protective equipment (PPE) and engineering controls.

4.4.1.2 Occupational Handler Non-Cancer Risk Characterization

The short- and intermediate-term toxicity endpoint effect (i.e., cholinesterase inhibition) selected for risk assessment is the same for both dermal and inhalation exposure. MOEs were derived based upon comparison of dermal exposure estimates against NOAELs of 50 mg/kg/day for both short- and

intermediate-term exposure. Both NOAELs were from a dermal toxicity study in the rabbit. MOEs were also derived based upon comparison of inhalation exposure estimates against a LOAEL of 0.1 mg/L (25.8 mg/kg/day) from a 90-day inhalation study in the rats. A common toxicological endpoint exists (cholinesterase inhibition) for the dermal and inhalation routes. However, because the uncertainty factors are dissimilar (i.e., 100 for the dermal route, and 1000 for the inhalation route), the MOEs were combined using the aggregate risk index (ARI) method. ARIs, which are ratios (of the MOE to the uncertainty factor) adjusted to a common denominator of 1, are calculated using the following formula:

ARI = 1 / {[1 / (Dermal MOE / Dermal UF)] + [1 / (Inhalation MOE / Inhalation UF)]}

An ARI is compared to an uncertainty factor of 1; an ARI of less than one is indicative of a risk concern for adverse health effects.

A detailed summary of the short-term and intermediate-term risk estimates for baseline, additional PPE, and engineering controls is presented in Table 17. It should be noted that estimated inhalation risk for all exposure time frames is a relatively minor component of the combined dermal and inhalation risk estimates expressed as ARIs. For example, most inhalation MOEs generally ranged from several thousand to over several million.

The **baseline** calculations indicate that the total ARIs are greater than, or equal to 1 (ARIs ranged from 1 to 48) and are **NOT** of risk concern for the following scenarios:

- (1d) mixing/loading liquids for dipping (ARI=6.3)
- (2) mixing/loading dusts for power duster or direct application (grain) (ARI=4.4)
- (4) applying sprays with an airblast sprayer (ag citrus fruit) (ARI=1)
- (5) applying sprays with a groundboom sprayer (all crops) (ARIs ranged from 1.8 to 48)
- (8) applying outdoor sprays with a thermal fogger (mosquitoes) (ARI=1)
- (14) mixing/loading/applying with a hose end sprayer (mushrooms) (ARI=3.2)
- (16) flagging aerial spray applications berries, ag (pumpkins), ag (veg), pine trees, mosquitoes, and ULV ag crops and ULV mosquitos) (ARIs ranged from 1.2 to 13).

For the remaining scenarios, ARIs are less than 1 and of risk concern at baseline exposure estimates.

The **personal protective equipment (PPE)** calculations for the scenarios requiring additional exposure reduction, indicate that the total ARIs are greater than, or equal to 1 (ARIs ranged from 1.0 to 29) and are **NOT** of risk concern for the following scenarios:

- (1a) mixing/loading liquids for groundboom application (all crops - *gloves only, no respirator*)
- (1b) mixing/loading liquids for aerial and chemigation application (ag pumpkins - *no respirator*, ag veg - *no respirator*, pine trees, mosquitoes - *no respirator*, and ULV ag crops).
- (1c) mixing/loading liquids for airblast sprayer (ag fruit & nut - *no respirator*, ag citrus fruit - *gloves only, no respirator*, and ornamentals - *gloves only, no respirator*).
- (1e) mixing/loading liquids for a thermal or non-thermal fogger (mosquitoes - *gloves only, no respirator*).
- (1f) mixing/loading liquids for handgun (turf - *gloves only, no respirator*).
- (4) applying sprays with an airblast sprayer (ornamentals).
  (11) applying handgun sprayer (turf - gloves only, no respirator).
- (12) mixing/loading/applying with a low pressure handwand (all crops - *gloves only, no respirator*).
- (13) mixing/loading/applying with a backpack sprayer (stored grain facility - *gloves only, no respirator,* agricultural premises - *gloves only, no respirator*, ornamentals - *no respirator*, and turf - *gloves only, no respirator*).

* Except where indicated in italics, additional PPE means double layer of clothing, chemical resistant gloves, and dust/mist respirator.

The **engineering control** calculations for scenarios requiring additional exposure reduction, indicate that the total ARIs are greater than, or equal to 1 (ARIs ranged from about 1 to 25) with additional **engineering controls** for the following scenarios:

- (1b) mixing/loading liquids for aerial and chemigation application (ag fruit & nut, turf and ULV mosquitos).
- (3a) mixing/loading wettable powders for groundboom application (berries).
- (3b) mixing/loading wettable powders for aerial application (berries).
- (3c) mixing/loading wettable powders for airblast sprayer (berries).
- (4) applying sprays with an airblast sprayer (berries).
- (6) applying sprays with a fixed-wing aircraft (all crops).
- (8) applying sprays with a fogger (non-thermal fogger for mosquitoes).
- (16) flagging aerial spray applications (turf and ULV mosquitoes).

The calculations of risk based on combined dermal and inhalation exposures expressed as an ARI are not greater than, or equal to 1 (the ARI was 0.94) despite the maximum mitigation measures for the following scenarios:

- (4) applying sprays with an airblast sprayer (ag fruit & nut) (ARI=0.94)

Note that risk concerns for this scenario may be moderated due to the closeness of the risk estimate to the target ARI and the use of maximum label rates in the calculations.

4.4.1.3 Occupational Handler Cancer Risk Characterization

Dermal and inhalation exposure to workers while handling malathion-containing products in occupational settings does not result in a cancer risk of concern. A summary of the cancer risk estimates for baseline, additional PPE and engineering controls for occupational handlers is presented in Table 18. Cancer risk estimates for occupational handlers were based on the unit risk, Q_1^* of 1.52×10^{-3} $(mg/kg/day)^{-1}$. This risk unit was used for assessing cancer risk for dermal and inhalation routes of exposure by conversion to oral equivalents using a 10% dermal absorption factor and a 100% inhalation factor. The calculations indicate that the total cancer risks are not greater than or approximately equal to 1.0×10^{-6} for any scenario when the necessary mitigation measures are applied. In general, a cancer risk of less than 1.0×10^{-6} does not trigger HED concern for worker exposure. An attempt is made to mitigate all worker cancer risks to at least 1.0×10^{-4}. In the summary in Table 18, it can be seen that all scenarios with risks at or above 10^{-4} are attempted to be lowered through additional PPE or engineering controls.

Data Gaps in Both Dermal and Inhalation Assessments: Dermal and inhalation risks could not be quantitatively assessed for four exposure scenarios because there are no appropriate chemical-specific or PHED data sets available. These scenarios are:

- (7) applying sprays with a helicopter (all crops)
- (9) applying dusts with a power duster; no PHED data exist.
- (10) dipping plants; no PHED data exist.
- (12) mixing/loading/applying with a backpack sprayer; no PHED data exist for baseline.

Data Quality and Confidence in Assessment: Several issues must be considered when interpreting the occupational exposure risk assessment. These include:

- Several handler assessments were completed using "low quality" PHED data. The resulting uncertainty means that the actual risks could be greater, or less than the risks estimated with these data.

- Several generic protection factors were used to calculate handler exposures. Specific mitigation measures may yield greater or less protection than is assumed. The ones used are considered to be reasonable high-end estimates.

- Factors used to calculate daily exposures to handlers (e.g., acres treated per day, square feet applied, and gallons of liquid applied) are based on the best professional judgement of HED staff.

- PHED mixer/loader data for wettable powder are used as a surrogate for dusts. While this is believed to be a reasonable fit, differences in particle size between dusts and wettable powder are possible and could lead to greater uncertainty in the exposure estimate.

- PHED applicator data for airblast are used as a surrogate for fogger.

Summary of Incidence Reports: As a result of its widespread use, there have been numerous incidences of malathion exposures and poisonings reported by various sources. These incidences and the sources from which they came are summarized below.

Sources of Information:

- OPP Incident Data System (IDS) - reports of incidents from various sources, including registrants, other Federal and state health and environmental agencies and individual consumers, submitted to OPP since 1992.

- Poison Control Centers (PCC) - as the result of Data-Call-Ins issued in 1993, OPP received Poison Control Center data covering the years 1985 through 1992 for 28 organophosphate pesticides, including malathion. This source includes information gathered from about 70 centers at hospitals and universities. In addition, OPP purchased data covering the years 1993 through 1996.

- California Department of Pesticide Regulation - California has collected uniform data on suspected pesticide poisonings since 1982. By law, physicians are required to report all occurrences of illness suspected of being related to pesticide exposure.

- National Pesticide Telecommunications Network (NPTN) - a toll -free information service supported by OPP receives and organizes information from the top 200 active ingredients for which telephone calls were received. Information is tabulated for categories of human incidents, animal incidents, calls for information, etc.

Incidences: Symptoms commonly reported for malathion exposure from the above sources cover the spectrum normally associated with organophosphate exposure, and include headache, nausea, dizziness, muscle weakness, drowsiness, difficult breathing, diarrhea, agitation, confusion, blurred vision and, death in certain intentional exposures (i.e., suicides). Nearly 70 separate incidences have been reported under IDS (some incidences involving multiple individuals). There were a total of 10,637 malathion cases in the PCC data base, of which, 564 were occupational exposure involving malathion alone. There were a total of 5,757 adult non-occupational exposures to malathion alone and another 3,371 exposures reported in children under age six. Compared to other organophosphate and carbamate insecticides, malathion had average or below average evidence of effects with the exception of life-threatening effects. The higher rate of life-threatening effects was based on a relatively small number of cases, two occupational and 11 non-occupational cases. From the California Illness Surveillance Program (1982 through 1995), malathion was judged to be responsible for the health effects seen in 395 cases, causing it to be ranked 6th as a cause of systemic poisoning in California from 1982 through 1994. From a review of these cases it was determined that the single largest cause of exposure was broken or leaking packaging of malathion.

Exposure to drift or odor from nearby application was the second most common cause. In Florida, for example, malathion was applied for Medfly in an area populated by 132,000 people in 1998. There were 34 cases classified as probable and 89 cases classified as possible pesticide-related illnesses resulting from this application. Most of the effects were likely due to a sensitivity to the irritant/allergic effects of malathion bait. On the list of the top 200 chemicals for which the NPTN received calls from 1984 - 1991 inclusively, malathion was ranked 4th with 900 incidents in humans reported. From April 1, 1995 through March 31, 1998, the NPTN received 95 reports of incidents from humans alleging adverse health effects from malathion. The most common complaints related to odors from spray drift or accidental spills that resulted in minor symptoms such as headache, nausea, and respiratory problems. A review of the literature found other reports of malathion cases; many of which involved accidental ingestion, extremely poor work practices, and intentional exposures to control head lice.

Conclusions: Much of the information presented above has inherent limitations, 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 in many cases may be a reaction to the odor rather than cholinergic poisoning. Nonetheless, symptoms brought on by odor effects are poisonings by definition. Broken bottles and other inadequate packaging accounted for over a quarter of the cases in California from 1982 through 1995. Drift and exposure to odors was the second most common cause of incidents in California. These latter typically resulted in mild and transient symptoms. In many cases it appears that symptoms are brought on by the offensive odor of the compound alone (i.e., cholinesterase depression need not be present). More serious malathion cases typically involve application by hand or backpack sprayer and direct exposure to concentrate. Often, serious exposures result from equipment failure such as hose breaks or failure to exercise minimal precautions during maintenance or clean-up. Though less hazardous than other organophosphates and carbamates on most measures, malathion has a higher incidence of life-threatening cases in Poison Control Center data for both children under age six and non-occupationally exposed adults. Extensive exposure to concentrates appears to be a likely risk factor in these cases.

4.4.2 Occupational Postapplication Exposures and Risks (Reentry Intervals)

EPA has determined that there are potential intermediate-term occupational postapplication exposures to individuals entering treated fields and contacting malathion and malaoxon residues on plant surfaces. Only postapplication dermal exposure has been assessed because postapplication inhalation exposure is expected to be negligible. Workers are expected, generally, to be performing activities (harvesting or non-harvesting) in malathion-treated fields for at least seven or more consecutive workdays in a growing season, with some fields receiving repeat malathion applications at 7-10 day intervals. Because of the seasonal nature of malathion use, a long-term exposure scenario is not expected for field workers. Mushroom houses are a special case, where the indoor, year long treatment and harvesting of multiple crop cycles result in the potential for mushroom house workers to experience long-term exposure to malathion (i.e. ≥180 days).

4.4.2.1 Postapplication Exposure Scenarios

The scenarios likely to result in postapplication exposure are as follows:

- Harvesting crops that have a high potential for dermal contact and all reentry activities associated with tree crops;
- Non-harvesting reentry activities with crops that have potential for a high degree of dermal contact;

- Harvesting and non-harvesting reentry activities with crops that have potential for a medium degree of dermal contact;
- Harvesting activities with crops that have potential for a low degree of dermal contact;
- Non-harvesting activities with crops that have potential for a low degree of dermal contact;
- Transplanting and pruning ornamental shrubs and trees.
- Harvesting, hand girdling, caning, tying, pruning, thinning, and tipping grapes.
- Mowing and maintaining turfgrass.
- Cutting, rolling and harvesting grass grown for sod.
- Harvesting mushrooms (short- intermediate- and long-term exposure).

Current labels include a 12 hour restricted entry interval (REI).

4.4.2.2 Data Sources and Assumptions for Postapplication Exposure

A transferable residue study (MRID 44113301) examined the level of malathion residues that could be transferred from treated turf following a single application of the 57EC formulation. At each of four diverse geographic locations, malathion was applied at 5 lb ai/A (4 quarts of formulated product in 100 gallons of water) using hand-gun spray equipment. Sprinkler irrigations were performed within one hour of each application, providing approximately 0.1 inch of water. At most locations, samples were collected before and after application, then at 4, 8, 12, 24, and 72 hours after treatment. The malathion parent compound was the analyte measured. Field recovery and laboratory recovery data were collected; however, storage stability samples were not examined. It was concluded that although this study only partially meets Subdivision K Pesticide Assessment Guideline criteria, none of the deficiencies preclude the use of the results from the turf study in this assessment.

A regression analyses of the measured values in the turf study was conducted to examine the dissipation data and to compare with the results of the study report. A summary of the reported (measured) values along with the predicted values is presented in the following table.

Summary of Malathion Dislogeable Foliar Residues from Turf.

Test Location	Transferable Residues ($\mu g/cm^2$)			Half-life (hours)	r^2 Value	Average Coefficient of Variation (CV)
	0 hours Posttreatment	12 hours Posttreatment	72 hours Posttreatment			
Pennsylvania	1.22 [0.648]	0.415 [0.325]	0.0110 [0.0103]	12.1	0.859	47.8
North Carolina	0.297 [0.0596]	ND [0.0284]	ND [0.000691]	11.2	1.000	45.4
Missouri	0.605 [0.0880]	0.0244 [0.0483]	<LOQ [0.00241]	13.8	0.830	71.1
California	0.815 [0.420]	0.536 [0.236]	0.0159 [0.0133]	14.5	0.827	51.5

[a] values in brackets are predicted transferable residues = exp (intercept + slope x time)
[b] <LOQ = less than limit of quantification
ND = No Data

While the average coefficient of variability from each individual site ranged from 45.4 to 71.1, suggesting considerable data variability among treated plots, R^2 values for each regression model (site) ranged from 0.827 to 1.000, which suggests good model prediction of residue levels. Regarding the latter, an R^2 value of 1.000 resulted from performing the regression analysis for just two data points from the North Carolina site. A rain event was partially responsible for limiting the data at this site.

The dissipation curve generated by the regression analysis of the measured values in the turf study allows for the prediction of DFR values beyond the period during which measurements were made and for application rates and crop activity transfer coefficients different from those for turf. The average half-life of malathion from the turf study was 13 hours. This corresponds to a 46% per day dissipation rate.

Although the daily dissipation rate may be estimated at 72%, the more conservative 46% per day dissipation rate was used for calculation of MOEs at various reentry intervals. The more conservative rate is used because the relationship between transferrable residues from the turf studies and dislodgeable foliar residues from agricultural crops is not fully known, and because the 13-hour rate more closely represents the dissipation expected to occur at the 12-hour REI currently appearing on malathion product labels. It should also be noted that in the turf study, the label-recommended use of irrigation shortly following the initial application was followed. This practice may result in diminishing the initial amount of residue available for transfer when compared to all other crops for which the data were used, and for which this practice is not followed. This uncertainty may add an underestimation component to the assessment.

DFRs were derived for harvesting and non-harvesting activities for other crops using appropriate standard TCs and the 46% dissipation rate rather than the standard 10% rate. Postapplication risks for turf used 1.3% of the application rate as the initial amount of residue available for transferring to skin, as predicted by the regression analysis based on the actual transferable residue value measured immediately after application (0 hour) in the turf study. For all other crop types, the HED standard value for initial DFR (20%) was used.

It should be further noted that this assessment of the potential postapplication exposure to malathion reflects residue of malathion *per se*. Information specific to the potential formation of malaoxon following uses subject to this reregistration action has not been submitted. Monitoring data used in the assessment of malathion bait spray in the California medfly eradication program (Bradman, M.A.,et al., 1994) indicates the postapplication formation of the oxidative breakdown product, malaoxon at levels an order of magnitude less than the parent compound on plant surfaces. Although aware of the possible formation of malaoxon following the uses subject to this reregistration action, there is insufficient information currently available to perform a quantitative exposure assessment without a large degree of uncertainty. Therefore, an assessment of the potential postapplication exposure to malaoxon has not been performed, and in order to do so would require the results from malathion/malaoxon residue dissipation studies for representative crops.

The following additional assumptions and factors were used to complete the postapplication exposure assessment:

- Harvesting reentry activity (harvesting) associated with applications to crops for which there is potential for a high degree of dermal contact (e.g. tomatoes), and all reentry activities (hand-harvesting, pruning, shaking, propping,) associated with applications to tree crops (e.g., apples, pecans and other such fruit and nut crops) at an application rate of 6.0 lb ai/acre: Tc = 10,000 cm^2/hour;

- Non-harvesting reentry activity (scouting, hoeing, staking, tying, weeding) associated with applications to crops for which there is potential for a high degree of dermal contact (e.g.,

tomatoes) at an application rate of 6.0 lb ai/acre: Tc = 4000 cm^2/hour;

- Harvesting (harvesting) and non-harvesting reentry activities (scouting, hoeing, weeding) associated with applications to crops for which there is potential for a medium degree of dermal contact (e.g., strawberries) at an application rate of 4.0 and 0.5 lb ai/acre: Tc = 4000 cm^2/hour;

- Harvesting reentry activity (harvesting) associated with applications to crops for which there is potential for a low degree of dermal contact (e.g., asparagus, broccoli and soybeans) at an application rate of 4.0 and 0.5 lb ai/acre: Tc = 2,500 cm^2/hour;

- Non-harvesting reentry activity (scouting, hoeing, irrigating, weeding) associated with applications to crops for which there is potential for a low degree of dermal contact (e.g., asparagus, broccoli and soybeans) at an application rate of 4.0 and 0.5 lb ai/acre: Tc = 1000 cm^2/hour;

- Transplanting and pruning reentry activity associated with ornamental shrubs and trees at an application rate of 2.6 lb ai/acre: Tc = 10,000 cm^2/hour;

- Harvesting, hand girdling, caning, tieing, pruning, thinning, and tipping grapes at an application rate of 2.0 lb ai/acre: Tc = 15,000 cm^2/hour; and,

- Mowing and maintaining turfgrass at an application rate of 8.7 lb ai/acre: Tc = 1000 cm^2/hour.

- Cutting, rolling and harvesting grass grown for sod at an application rate of 8.7 lb ai/acre: Tc = 10,000 cm^2/hour.

- Cutting and harvesting reentry activity associated with applications to mushrooms at an application rate of 2 lb ai/acre: Tc = 2500 cm^2/hr.

The DFR is derived from the application rates for these crops, using an estimated 1.3 percent of the rate applied as initial dislodgeable residue for turf uses (based on predicted residue value at time 0 in the turf study), 20 percent of the rate for all other use sites, and an estimated 46 percent dissipation rate per day (based on reported residue values from the turf study) for all use sites.

4.4.3.3 Occupational Postapplication Risk Characterization

Short-, Intermediate-, and Long-term Non-cancer Risk Estimates: MOEs for various restricted entry intervals (REIs) were derived by a comparison of dermal exposure estimates against a NOAEL of 50 mg/kg/day for intermediate term exposure or a NOAEL of 2.4 mg/kg/day for long-term exposure. The intermediate term NOAEL was from a dermal toxicity study in the rat. The long-term NOAEL was from an oral study; thus, a 10% dermal absorption factor was applied to long-term exposure. An MOE of $\geq$100 is generally considered to be less than HED's level of risk concern for postapplication exposure to malathion.

Based on the occupational postapplication risks determined by the surrogate agricultural assessment, reentry is of concern on the same day as application (12 hours following treatment) for all exposure scenarios except for non-harvesting activities associated with crops for which there is potential for a low degree of dermal contact (e.g., asparagus, broccoli and soybeans) at the 0.5 lb ai/acre rate, and for all reentry activities associated with mowing and maintaining turfgrass. REIs, where the margins of exposure

are NOT of concern for workers, are estimated to range from 1 to 6 days. Because crops treated with malathion have an existing REI of 12 hours, HED has a concern over occupational short-term occupational postapplication risk.

The only chronic occupational postapplication scenario is for handling mushrooms (cutting, harvesting, sorting and packing) from beds that have been treated with malathion. It is assumed that a worker is engaged in such work for 180 days per year. The long-term endpoint is a 2.4 mg/kg/day NOAEL from a from a two-year feeding study. A dermal equivalent dose (using a 10% dermal absorption factor) of 40 mg/kg/day was used in the calculation. The resulting chronic surrogate postapplication assessment for malathion indicates that:

- MOEs equal or exceed 100 (i.e., 119) for harvesting activities associated with applications to mushrooms on the **3rd day** following application at a rate of 2.0 lb ai/acre: Tc = 2500 cm^2/hr.

Therefore, the current REI of 12 hours is not sufficiently protective. A 3 day REI is necessary to reach the target MOE of 100.

Postapplication Cancer Risk Estimates: Cancer risk estimates for occupational handlers were based on the unit risk, Q1* of 1.52×10^{-3} $(mg/kg/day)^{-1}$. The target for worker risk is 1.0×10^{-6}.

Based on the occupational postapplication risks determined by the surrogate agricultural assessment, reentry is of concern on the same day as application (12 hours following treatment) for all exposure scenarios except for non-harvesting activities associated with crops for which there is potential for a medium degree of dermal contact at the 0.5 lb ai/acre rate; non-harvesting activities associated with crops for which there is a low degree of dermal contact (e.g., asparagus, broccoli and soybeans) at the 0.5 lb ai/acre rate, and for activities associated with mowing and maintaining turfgrass. REIs, where the margins of exposure are NOT of concern for workers, are estimated to range from 1 to 5 days. Because crops treated with malathion have an existing REI of 12 hours, HED has a concern over occupational postapplication cancer risk. However, short- and intermediate-term toxicity endpoints drive the ultimate determination of postapplication risk and reentry intervals for malathion, not the cancer risk described above.

Summary of Malathion Occupational Post-Application Exposure and Risk Estimates						
Crops[1]	Application Rate[2] (lb ai/acre)	REI where MOE[3] ≥ 100		REI where cancer risk[6] ~1.0e-06		Current REI[7]
		Non-harvesting[4]	Harvesting[5]	Non-harvesting[4]	Harvesting[5]	
Crops with Potential for High Degree of Dermal Contact (i.e., apples, avocado, chestnuts, cherries, corn, figs, grapefruit, lemon, lime, nectarines, pecans, tomatoes,	6.0	5 days	6 days	3 days	5 days	12 hours
Crops with Potential for Medium Degree of Dermal Contact (e.g., beans, blackberries, boysenberries, cotton, dewberries, eggplant, gooseberries, loganberries, melons, raspberries, squash, strawberries, walnuts	4.0	4 days	4 days	3 days	3 days	12 hours
Crops with Potential for Medium Degree of Dermal Contact (see list above)	0.5	1 day	1 day	same day	same day	12 hours
Crops with Potential for Low Degree of Dermal Contact (e.g., alfalfa, asparagus, barley, garden beets, broccoli, cabbage, celery, lettuce, oats, onions, peas, pineapple, rye, soybeans, wheat	4.0	2 days	3 days	same day	same day	12 hours
Crops with Potential for Low Degree of Dermal Contact (see list above)	0.5	same day	same day	same day	same day	12 hours
Transplanting/pruning Ornamental Trees and Shrubs (e.g., Christmas tree plantations and nursery stock)	2.6	5 days	5 days	3 days	3 days	12 hours
Harvesting, Girdling, Caning, Tieing, Pruning, Thinning and Tipping Grapes	2.0	5 days	5 days	4 days	4 days	12 hours
Maintaining and Harvesting Turfgrass (e.g., turf in parks, sod farms and golf courses)	8.7	same day	2 days	same day	1 day	12 hours
Cutting and Harvesting Mushrooms	2.0	3 days	3 days	1 day	1 day	12 hours

1 Crop listing is not all inclusive of registered use sites, but it includes most crops which are representative of the categories with which they appear above. Default transfer coefficients were used for the above categories according to HED Science Advisory Council Policy.003 (May 7, 1998).

2 Maximum application rates were used in the assessment. For crops with medium and low potential for dermal contact, the lowest rate for the crop grouping was also included to help indicate a range of possible exposures.

3 The target Margin of Exposure is 100 for dermal exposure.

4 Non-harvesting activities include scouting, hoeing, staking, tying, weeding, etc.

5 It is important to note that for those crops which are mechanically harvested, negligible exposure is considered likely, except for any ancillary manual activities associated with the process. These latter activities must be considered in the exposure assessment. For example, this may apply to almonds and other tree nut crops where the use of mechanical blowers to move fallen nuts into wind rows can present potentially high post-application exposures.

6 The Agency's target cancer risk is >1.0e-06. The REIs listed here have associated risks that are close to this target.

7 Set as interim REIs based on the criteria of the Agency's Worker Protection Standards.

4.4.3 Residential Handler Exposure

Malathion is a common home/garden use product. Several malathion-containing consumer products also contain other active ingredients such as captan and methoxychlor. Consumer products are available as ready-to-use liquids, wettable powders, and dusts for insect control on fruits, vegetables, ornamentals, and lawns. Malathion is also used as an outdoor premise spray to control insect pests such as fleas, houseflies, and mosquitoes. Application is typically by sprays to home orchards, herbaceous and woody ornamentals, vegetables and small fruits. Malathion is applied by dust shaker can, garden hose end sprayer, low pressure handwand, and backpack sprayer.

According to the National Home and Garden Pesticide Use Survey Final Report, Volume 1 (March, 1992), the major use of malathion in the home garden is on roses and other ornamentals (about 42%), followed by edible food crops (about 25%), and lawns (about 18%).

Residential handler exposure to malathion residues via dermal and inhalation routes can occur during handling, mixing, loading, and applying activities. The exposure duration of these activities is classified as short-term (1-7 days) based on label directions for multiple applications which may be made every 7 days "as necessary". The frequency of use by residential handlers is not expected to result in continuous exposure durations of 1 week to several months or longer, such that intermediate-term or long-term residential exposure assessments would be needed.

4.4.3.1 Residential Handler Exposure Scenarios

HED has determined that there is potential exposure to residential mixer, loader, and applicators during the usual use-patterns associated with malathion. Based on the use patterns, five major residential exposures were identified for malathion:

(1a) mixing/loading/applying liquid with a low pressure handwand;
(1b) mixing/loading/applying wettable powder with a low pressure handwand;
(2) mixing/loading/applying liquid with a hose end sprayer;
(3) mixing/loading/applying liquid with a backpack sprayer;
(4) mixing/loading/applying liquid with a fogger; and
(5) mixing/loading/applying dust using a shaker can.

4.4.3.2 Residential Handler Exposure Data Sources/Assumptions

Residential handler exposure assessments were completed by HED assuming an exposure scenario for homeowners wearing the following attire: short sleeved shirt, short pants, shoes and socks, and no gloves or respirator. PHED values used to estimate daily unit exposure values were taken from the *Standard Operating Procedures (SOPs) for Residential Exposure Assessments (December 1997).*

No exposure data sets for application with a fogger or a dust shaker can are available in PHED. However, the scenario for mixing/loading and applying liquids for mosquito control with a backback sprayer is considered a reasonable surrogate for fogger use. The application rate and amount handled are virtually the same. Further, results from the backpack analysis are considered an upper bound for fogger because the former includes manual application, whereas the latter involves only activating the aerosol generator and leaving the area. Inhalation exposure from aerosol-generated malathion is covered under residential postapplication exposure. For the shaker can scenario, the exposure estimate was made using the assumption from the draft Residential SOPs that handlers are exposed (dermal and inhalation) to 10% of the active ingredient applied.

The area treated per day was assumed to be 1,000 ft^2 for spot treatment of homeowner turf. The amount handled per day was assumed to be 5 gallons of spray for low pressure handwand and backpack sprayers and 50 gallons of spray for hose end sprayers. Calculations were made using the maximum application rates for crops as stated on the available malathion labels. Application rates represent the range of exposure levels associated with the various use patterns.

For purposes of cancer risk estimates, an internal or absorbed daily dose is amortized over an individual's lifetime. It was assumed that the residential handler would be exposed to malathion 5 days per year for 50 years over a 70 year lifetime.

4.4.3.3 Residential Handler Risk Characterization

Short-term margins of exposure (MOEs) for residential handlers were derived based upon comparison of dermal exposure estimates against a NOAEL of 50 mg/kg/day for short-term exposure. The short-term NOAEL is from a route-specific dermal toxicity study. Therefore, it was not necessary to apply a dermal absorption factor. MOEs were also derived based upon comparison of inhalation exposure estimates against a LOAEL of 0.1 mg/L which translates to 25.8 mg/kg/day. **The uncertainty factors and target MOEs for residential populations (including the 1x FQPA safety factor) are 100 for short-term dermal risk and 1000 for short-term inhalation risk.** Because the adverse effect of concern (cholinesterase inhibition) is the same for both dermal and inhalation exposure, it is appropriate to consider the total risk contribution from both exposure routes. However, because the target dermal MOE is 100 and the target inhalation MOE is 1000, MOEs for both routes of exposure were calculated separately and the total risk was estimated by an Aggregate Risk Index (ARI). An ARI of less than one is indicative of a risk concern for adverse health effects.

Cancer risk estimates for residential handlers were based on the unit risk, Q_1^*, of 1.52×10^{-3} $(mg/kg/day)^{-1}$. This risk unit was used for estimating cancer risk from dermal and inhalation routes of exposure by conversion to oral equivalents using a 10% dermal absorption factor and a 100% inhalation factor. In general, a cancer risk of less than 1.0×10^{-6} does not trigger HED concern for residential handler exposure.

As shown in Table 19, short-term dermal and inhalation exposures result in ARI values that exceed HED's level of concern for two of the five residential handler scenarios: the **ARI is 0.5** for mixing/loading/applying liquid with a low pressure handwand (mosquitoes/household pests) and the **ARIs range from 0.02 to 0.7** for mixing/loading/applying with a hose end sprayer (fruit trees, ornamentals, and mosquitoes/household pests). It should be noted that ARIs of risk concern are driven by dermal exposure (dermal MOEs range from 15 to 69); inhalation exposure contribution to total risk is minimal. A third scenario, for which only dermal exposure and risk was estimated, mixing/loading/and applying dust with a shaker can, yields **dermal MOEs ranging from <1 to 2** (target MOE=100) which exceed HED's level of concern.

With the exception of the shaker can uses, cancer risk estimates for residential handlers are in the **10^{-7} to 10^{-9}** range and do not exceed HED's level of concern. The shaker can uses are of risk concern: handler dermal exposure alone results in a cancer risk estimates in the **10^{-5} range**.

4.4.4 Residential Postapplication Exposures and Risks

HED has determined that there is potential for non-occupational postapplication exposures to malathion residues from the following sources: 1) outdoor use of malathion-containing consumer products by residential handlers; 2) commercial use of malathion at residential sites, "pick-your-own" strawberries or other orchards, public access areas such as parks, golf courses, recreational areas, and playgrounds; and 3) public health use of malathion for wide area mosquito control.

HED considers the potential for dermal contact (adults and children) with malathion residues on residential turf, in the home orchard, vegetable or ornamental garden while playing on the lawn, working in treated vegetable gardens, harvesting from fruit and nut trees, pruning or thinning ornamental trees or shrubs and harvesting strawberries in commercial "pick-your-own" fields to be the most common exposure scenarios and the ones most likely to bracket the overall risk. The inhalation component of postapplication exposure in these scenarios is believed to be negligible and is therefore not included in the determination of postapplication risk for residential exposure sources. However, the inhalation component of postapplication exposure has been included for public health uses and is fully described below.

HED has determined that there are potential postapplication exposures to adults and children resulting from public health use of malathion for mosquito control. These potential exposures are estimated because of the concern for the residues that may be deposited during the ultra low volume (ULV) aerial and ground-based fogger applications in the vicinity of residential dwellings. The assessment has been developed to ensure that the potential exposures are not underestimated and to represent a conservative model that encompasses potential exposures received in other recreational areas (e.g., school playgrounds, parks, athletic fields). Because ULV ground-based fogging operations may result in inhalation exposure to individuals in the immediate vicinity of these applications, a separate estimate of the risk from this potential exposure route is also provided even though it is not considered to be a major contributor to the hazard.

HED believes it is reasonable to expect dermal, inhalation, and inadvertent oral exposure from the public health use, as well as postapplication dermal and inadvertent oral exposure from outdoor use of malathion-containing consumer products in a residential setting to occur in a single day. Thus, HED has selected certain non-occupational exposure scenarios for purposes of developing aggregate exposure estimates.

4.4.4.1 Postapplication Exposure Scenarios

The scenarios likely to result in dermal (adult and child) and incidental non-dietary (child) postapplication exposures are as follows:

- Dermal exposure from residues on vegetable/small fruit gardens;
- Dermal exposure from residues on fruit trees and ornamentals;
- Dermal exposure from "pick your own" strawberries;
- Dermal exposure from residues on commercially treated residential turf (adult and toddler);
- Incidental nondietary ingestion of residues on commercially treated lawn (residential, park and school playground) from hand-to-mouth transfer (toddler);
- Ingestion of treated commercially treated turfgrass (residential, park and school playground) (toddler); and
- Incidental ingestion of soil from commercially treated areas (residential, park and school playground) (toddler).

The scenarios likely to result in dermal, inhalation (ground-based ULV), and incidental non-dietary postapplication exposures resulting from mosquito-borne disease control uses are as follows:

- Dermal exposure from residues deposited on turf at residential, park, and school sites (adult and toddler);
- Incidental nondietary ingestion of residues deposited on turf at residential, park, and school sites from hand-to-mouth transfer (toddler);
- Ingestion of treated turfgrass (toddler); and
- Incidental ingestion of soil from treated areas (toddler).

4.4.4.3 Data Sources and Assumptions for Residential Postapplication Exposure

Residential exposures were assessed for both adults and toddlers based on guidance provided in the *Draft: Standard Operating Procedures (SOPs) for Residential Exposure Assessment (12/11/97 Version).* Additionally, foliar dissipation data submitted in support of reregistration; human exposure and deposition data from published literature sources; and modeled estimates of deposition using *AgDRIFT* (V. 1.03 -- June 1997 developed by the *Spray Drift Task Force (SDTF))* were utilized to generate postapplication exposure estimates.

The results of a transferable residue study on turf (MRID 44113301) discussed in Section 4.4.2 was used in the same manner as described for the occupational postapplication assessment. The dissipation curve generated by the regression analysis of the measured values in the turf study allows for the prediction of DFR values for all non-occupational exposure scenarios. The average half-life of malathion from the turf study was 13 hours. Postapplication exposures involving contact with turf were based on an initial amount of residue available to transfer to the skin predicted by the regression analysis (i.e., 1.3% of the application rate) which included the actual transferable residue value measured immediately after application (0 hour) in the turf study. For activities involving contact with plant surfaces other than turf (ornamentals, fruit trees, etc.), HED's standard value of 20% of the application rate was assumed for the amount of residue initially available for transfer to skin.

Chemical-specific data for ULV public health mosquito control uses of malathion have not been submitted by the registrant. Therefore, the equations and assumptions used for each of the scenarios were derived from airborne exposure models, and taken from published literature studies and the Draft Standard Operating Procedures (SOPs) for Residential Exposure Assessments guidance document. A detailed description of the literature studies, the model and the assumptions and equations are provided in the Occupational and Residential Exposure Assessment (J. Arthur, 9/16/99).

<u>Published Literature Studies - Ground-based ULV</u>
Two published literature studies reflecting ground-based ULV applications with malathion provide human exposure and deposition data (Tietze et al., 1994 and Moore et al., 1993). After considering the data that

are available in the Tietze *et al.* and Moore *et al.* papers, an off-target deposition rate of **5 percent of the application rate** was used by HED to evaluate ground-based ULV applications. A value slightly higher than the mean values for both studies was selected because of the variability in the data and the limited number of data points. Thus, the amount of residue on turf resulting from ground-based ULV application and available for dermal transfer is estimated as follows:

> amount available for transfer = amount deposited x amount dislodgeable (1.3%), where amount deposited = application rate x deposition rate (5%).

Airborne Exposure Models - Aerial ULV

Data similar to that for ground applications discussed above were not available for the aerial deposition. Therefore, in order to calculate deposition from aerial ULV applications, HED used *AgDRIFT* (V 1.03 -- June 1997) which is the model that was developed as a result of the efforts of the *Spray Drift Task Force (SDTF).* AgDRIFT is capable of producing a variety of useful outputs. The key for HED in this assessment was to determine from the model what percentage of the application volume remained aloft and what percentage of the resulting droplets deposited on the surfaces in the treatment area as well as downwind from the treatment area. AgDRIFT is generally intended to calculate deposition rates in areas that are downwind from the treatment area (i.e., presented from the border of the treatment area to areas of interest downwind). HED has used the values at the border of the treatment area to represent the deposition rate within the treated area. It was determined that from the edge of the treatment area to 1000 feet downwind, approximately **35 percent of the theoretical application is deposited**. This value is intuitively consistent with what one might suspect would occur considering the agricultural engineering parameters associated with malaria vector applications. Thus, the amount of residue on turf resulting from aerial ULV application and available for dermal transfer is estimated as follows:

> amount available for transfer = amount deposited x amount dislodgeable (1.3%), where amount deposited = application rate x deposition rate (35%).

Deposition from aerial ULV applications is assumed to be uniform throughout the drift zone even though AgDRIFT indicates minor fluctuations in the region of interest. The deposition region of interest has been defined as the region immediately adjacent to the treatment area out to a reasonable model approximated limit (i.e., for aerial -- about 2000 feet). After the deposition factors were determined, postapplication exposure values were calculated using appropriate surrogate exposure values, label stipulated application rates, and application rates based on available use information.

The following additional general assumptions were made for all scenarios:

- Postapplication was assessed on the same day the pesticide is applied because it was assumed that the homeowner could be exposed to gardens, fruits and nuts, ornamental shrubs, flowers, trees, and turfgrass immediately after application. Therefore, postapplication exposures were based on day 0.

- Adults were assumed to weigh 70 kg. Toddlers (3 years old), used to represent the 1 to 6 year old age group, were assumed to weigh 15 kg.

- The maximum labeled application rate (ULV) for aerial mosquito control is 0.23 lb ai/acre. The maximum labeled application rate (ULV) for ground-based fogger mosquito control is 0.11 lb ai/acre. (based on FYFANON® ULV label. EPA Reg. No. 4787-8)

- The dermal transfer coefficient which is the basis for the toddler calculation is based on a Jazzercise activity which is generally considered to represent a bounding estimate of dermal exposure. Another conservative aspect of the postapplication calculation is the

duration in which exposed populations are assumed to be in contact with treated turf on a daily basis (i.e., 4 hours/day for adults and 2 hours/day for toddlers -- both upper percentile estimates based on data available in the *EPA Exposure Factors Handbook*).

Additional parameters that effect residue transfers from surface-to-skin, skin-to-mouth, and object-to-mouth activities for adults and/or children are as follows:

Surface-to-skin residue transfer (adult and toddler)
Residue source: turf exposure time = 2 hours per day; TC = 43,000 cm2/hr (adult) and 8,700 cm2/hr (toddler)
Residue source: garden and tree foliage exposure time = 0.67 hours per day; TC = 10,000 cm2/hr (adult)

Skin-to-mouth residue transfer (toddler)
residue source: plant surface residue transfer to the hand and to the mouth
The mean surface area of both hands was assumed to be 350 cm2 for a toddler (age 3 years); replenishment of the hand with pesticide residues was assumed to be an implicit factor; it was assumed that there is a n-to-one relationship between the dislodgeable residues on the turf and on the surface area of the skin after contact.

residue source: soil particles transfer from the hand to the mouth
On the day of application, it was assumed that 100% of the application rate is available in the uppermost 1 cm of soil; the assumed ingestion rate for children ages 1-6 is 100 mg/day

Object-to-mouth residue transfer (toddler)
residue source: grass surface
The assumed ingestion rate for grass for toddlers (age 3 years) was 25 cm2/day. This value is intended to represent the approximate area from which a child may grasp a handful of grass.

4.4.4.4 Residential Postapplication Risk Characterization

Postapplication Non-Cancer Risk Estimates: The detailed results of the short- and intermediate-term residential postapplication exposure/risk assessment is presented in Table 20 and summarized here. MOEs for four adult and one toddler postapplication dermal exposure scenarios ranged from 31 to 63 and, thus, exceed HED's level of concern. These scenarios are:

- Dermal exposure to residues on turf following application with handgun sprayer by commercial applicator (adult and toddler);
- Dermal exposure to residues on vegetables/small fruit gardens, fruit trees, and ornamentals following homeowner spray applications (adult) and in "pick-your-own" strawberries (adult).

MOEs for all other scenarios substantially exceed the target MOE of 100 (600 to >860,000) and are not of risk concern. Public health uses (ground and aerial ULV application) result in dermal MOEs that are >3,400 for toddlers and adults and incidental oral ingestion MOEs that are >25,000 for toddler's hand(object)-to-mouth activities.

Postapplication Cancer Risk Estimates: The results of the residential postapplication exposure/risk assessment for cancer are presented in Table 21. Postapplication dermal contact with turf following treatment by handgun application, contact with vegetables and small fruit gardens, and contact from "pick-your-own" strawberries all have risk slightly above the cutoff point of 1.0e-06 for Agency concern. Dermal postapplication exposure from contacting turf following aerial or ground-based ULV mosquito control is well below the cutoff point; as is contact with treated fruit trees and ornamentals.

Since the risk of cancer increases with duration and frequency of exposure, the cancer risks below were estimated for adults who are exposed to the same pesticide, malathion in this case, for fifty years out of their lifetime. This is considered to be a conservative approach. The cancer process is not fully understood with regard to shorter term exposures, especially regarding early childhood exposure. While the same exposure represents a larger dose to a child (age 1 to 6) than to an adult, as mentioned earlier, at present the Agency does not have a methodology to derive a meaningful estimate of cancer risk to toddlers. However, it is believed that the fifty-year duration of exposure used in the estimation of cancer risk for adults may present a worst case scenario.

***Postapplication Inhalation Exposure/Risk from Ground-based Truck Fogger Application*:**
As mentioned earlier, inhalation exposure usually does not factor significantly into postapplication risk. However, due to the major use of malathion in ULV aerial and truck fogger applications to control mosquitoes, a risk assessment has been developed below for residential exposure to a ground-based truck fogger. The ground-based fogger is believed to be a more conservative model for exposure estimation than the aerial ULV application because of the very large dilution factor associated with the latter. The approach is based on the one described in the Draft Standard Operating Procedures (SOPs) for Residential Exposure Assessment for inhalation exposure to outdoor residential short-term pest control. The major difference is that the SOPs begin assuming the use of a commercial fogger product that has a known volume. In the scenario below, the beginning assumption is that a ground-based fogger truck releases its full application rate into the breathing zone of the residential bystander, thus turning an application rate expressed as lbs. ai/ft^2, into a concentration expressed as the same amount (lbs) of ai, only on a per cubic foot (ft^3) basis. The following is a stepwise process, including assumptions and calculations for estimating residential bystander inhalation exposure to a truck fogger.

The following inputs, assumptions, and calculations were used to estimate inhalation exposure and risk resulting from ground-based ULV applications:

Inputs and Assumptions

- Ground-based ULV truck fogger application rate is 0.11 lb ai/acre
- Dilution of airborne concentration of 1 to 100 (i.e., 1 percent (0.01) of product released is available for exposure
- Adult breathing rate = 0.55 m^3/hour, and weight is 70 kg; toddler breathing rate = 0.36 m^3/hour, and weight is 15 kg
- Exposure time is 20 minutes (0.33 hours)
- Target MOE = 1000
- Short- and intermediate-term Inhalation LOAEL = 25.8 mg/kg/day
- Cancer risk, $Q1^* = 1.52e^{-03}$ $(mg/kg/day)^{-1}$
- Target cancer risk $\leq 1.0e^{-06}$

Calculations for short- and intermediate-term risk

- Application rate of 0.11 lb ai/acre x 1 acre/43,560 ft^2 = 0.0000025 lbs ai/ft^2
- Expressed as an airborne concentration = 0.0000025 lbs ai/ft^3
  0.0000025 lbs ai/ft^3 x 35.3 ft^3/1 m^3 = 0.000088 lbs ai/m^3
  0.000088 lbs ai/m^3 x 454,000 mg/lb = 39.95 mg/m^3
- Application concentration (39.95 mg/m^3) x dilution factor (0.01) = 0.4 mg/m^3
- $Dose_{adult}$ = (concentration) x (breathing $rate_{adult}$) x (exposure duration) ÷ BW_{adult}
  = (0.4 mg/m^3) x (0.55 m^3/hour) x (0.33 hours/day) ÷ 70 kg = 0.001 mg/kg/day

- **Short- and Intermediate-term $Risk_{adult}$ = MOE = $LOAEL_{inhal.}/Dose_{adult}$**
  = (25.8 mg/kg/day)/(0.001 mg/kg/day) = 25,800

- $Dose_{toddler}$ = (concentration) x (breathing $rate_{toddler}$) x (exposure duration) ÷ $BW_{toddler}$
  = (0.4 mg/m^3) x (0.36 m^3/hour) x (0.33 hours/day) ÷ 15 kg = 0.003 mg/kg/day

- **Short- and Intermediate-term $Risk_{toddler}$ = MOE**
  = (25.8 mg/kg/day)/(0.003 mg/kg/day) = 8,600

Calculations for cancer risk

- **Cancer $risk_{adult}$** = $Dose_{adult}$ x (5 days exposure/365 days a year) x (50 years exposure/70 year lifetime) x (Q1*)
  = (0.001 mg/kg/day) x (0.01) x (0.01) x (0.7) x (0.00152) = **$1.06e^{-8}$**

Both adult and toddler risk estimates for short-term inhalation exposure do not exceed the level for Agency concern for inhalation exposure to truck foggers. Cancer risk for adults also does not trigger Agency concern. Methodology for making a meaningful determination of cancer risk to toddlers is not yet developed by the Agency. It is important to note also that the above risks are based on conservative assumptions regarding the circumstances of exposure (i.e., standing for 20 minutes in the direct off-loading of a fogger truck as it passes by). These inhalation risks are aggregated with dermal risks from the same exposure scenario in a later section. It should be noted that this truck fogger assessment represents a worst-case for ground-based fog mosquito control scenarios, and therefore a postapplication inhalation exposure scenario for small, homeowner-operated aerosol generators was not included this report. A calculation of postapplication inhalation risks for this latter application, and using methodology in the Draft SOPs for Residential Exposure Assessments, results in MOEs exceeding 5.0 x 10^{-06}.

4.4.4.5 Non-occupational Exposure Aggregation

HED believes there is potential for non-occupational exposure to malathion from dermal, inhalation, and non-dietary oral contact with various exposure media in residential settings. Such exposures are expected to occur during activities that would reasonably be expected to occur on the same day. Thus, certain residential exposure scenarios (application + postapplication) have been considered for aggregation and assessments were conducted for both adults and toddlers.

For adults, aggregate exposure must consider the potential for both handling/applying the pesticide, as well as, the potential postapplication contact. For toddlers, only postapplication is relevant, however, certain age specific differences, like hand-to-mouth activity and body weight must be considered here, as well. As was mentioned earlier, a method for making a meaningful estimate of cancer for children has not yet been developed, and thus does not appear in the aggregate assessment below.

4.5 Cumulative Exposure

It has been determined that the organophosphates (OPs) share a common mechanism of toxicity: the inhibition of cholinesterase levels. As required by FQPA, a cumulative assessment will need to be conducted to evaluate the risk from food, water and non-occupational exposure resulting from all uses of OPs. Currently, the Agency is developing the draft methodology needed to conduct such an assessment with guidance/advice provided by the Science Advisory Panel. It is anticipated that this draft methodology will be available for comment and scientific review in 1999. Consequently, the risks summarized in this document are only for malathion.

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5.0 AGGREGATE RISK ASSESSMENTS AND RISK CHARACTERIZATION

5.1 Acute Aggregate Risk

Acute aggregate risk estimates do not exceed HED's level of concern. The aggregate acute dietary risk estimates include exposure to combined residues of malathion and malaoxon residues in food and water and does not include dermal and incidental oral exposure. Exposure (food only) to combined residues of malathion and its malaoxon metabolite, based on an upper-bound analysis using tolerance-level residues and assuming 100% of crop treated, represents 38% of the acute PAD for the most highly exposed population subgroup (children 1-6 years). Exposure to all other groups represents less than 35% of the acute PAD. Using conservative screening-level models, the estimated maximum peak concentrations of malathion and malaoxon in surface water is 322 μg/L. This estimated peak concentration is considerably less than HED's drinking water level of comparison for exposure to malathion in drinking water as a contribution to aggregate acute dietary risk. Based on the available information, HED concludes with reasonable certainty that no harm to any population will result from acute dietary exposure to malathion.

5.2 Short- and Intermediate-Term Aggregate Risks

Short-term aggregate risk estimates exceed HED's level of concern. Currently registered uses of malathion in residential settings result in dermal, inhalation, and inadvertent oral exposures that alone exceed HED's level of concern. Any additional exposure through food or drinking water would contribute to an already unacceptable risk estimate.

5.3 Chronic (Non-Cancer) Aggregate Risk

Chronic (non-cancer) aggregate risk estimates do not exceed HED's level of concern. The aggregate chronic dietary risk estimates include exposure to combined residues of malathion and malaoxon in food and water. No chronic residential use scenarios were identified. Exposure (food only) to combined residues of malathion its malaoxon metabolite, based on a Tier 3 refinement using USDA/PDP and FDA monitoring data, average residues from field trials, and percent of crop treated data, represents 4% of the chronic PAD for the most highly exposed population subgroup (children 1-6 years). Exposure to all other groups represents less than or equal to 4% of the chronic PAD. Using Tier 1 screening-level models, the estimated 56-day average concentration of malathion and malaoxon in surface water is 97μg/L. The value used for comparison to the DWLOC is 32 μg/L (97μg/L./3 = 32 μg/L). This estimated average concentration is considerably less than HED's drinking water level of comparison for exposure to malathion in drinking water as a contribution to aggregate chronic dietary risk. Based on the available information, HED concludes with reasonable certainty that no harm to any population will result from chronic dietary exposure to malathion.

5.4 Aggregate Cancer Risk

Aggregate cancer risk estimates exceed HED's level of concern. Currently registered uses of malathion in residential settings result in dermal and inhalation exposures that alone exceed HED's level of concern. Any additional exposure through food or drinking water would contribute to an already unacceptable risk estimate.

6.0 CONFIRMATORY DATA

Additional data requirements have been identified in the referenced Science Chapters and are summarized here.

Toxicology Data for OPPTS Guidelines:

Two new toxicity studies have been required to fully comply with guideline requirements and to provide better hazard characterization: 1) a 90-day feeding study in dogs because the available 1-year study is unacceptable, and 2) a 90-day inhalation study in rats because the available 90-day study did not establish a NOAEL. In addition, the Agency has recently issued FR42945 (August 6, 1999) requiring registrants of neurotoxic pesticides to conduct acute, subchronic, and developmental neurotoxicity studies. Thus, a developmental neurotoxicity study for malathion will be required under this Data Call-in program.

Product and Residue Chemistry Data for OPPTS Guidelines:

The existing product and residue chemistry data base for malathion is substantially complete. These data are sufficient to reassess most tolerances and to conduct a reliable dietary (food source) risk assessment. Although a number of guideline requirements have been satisfied since the completion of the Product and Residue Chemistry Chapters in 6/99 and 4/99, respectively, some data remain outstanding. The absence of these required data does not impinge on the Agency's conclusions regarding which uses are eligible for reregistration. The current outstanding data requirements are included below.

860.1500 Crop Field Trials

Leafy Vegetables (Except Brassica Vegetables) Group: Celery
To support and /or maintain the existing crop group tolerance for leafy vegetables (except Brassica vegetables), additional data are required. Data depicting residues of malathion and malaoxon in/on celery following application of an appropriate EC formulation according to the maximum proposes/registered use patterns. The number of field trails and geographic locations of trial sites should be in compliance with the current guidance.

Apples
The apple data submitted by IR-4 and reflecting six apple field trials are inadequate because of meager geographic representation. Additional apple field trials must be conducted. The required field trials should be conducted in major U.S. apple-growing regions according to the maximum use pattern (i.e., five foliar applications, with a 7- to 11-day retreatment interval, of a representative EC formulation at 1.25 lb ai/A/application using ground equipment) the registrant(s) wishes to support.

Quince
Apple field trial data may be translated to quince. When adequate apple data have been submitted and evaluated, label revisions will be required to make the use patterns for quince consistent with apple.

Barley hay and straw
The available data pertaining to malathion residues of concern resulting from preharvest applications on wheat grain may be translated to barley grain, oat grain, and rye grain. The available data pertaining to malathion residues of concern resulting from preharvest applications on wheat forage and straw may be translated barley straw, oat forage and straw, and rye forage and straw. The requested data for wheat hay may be translated to barley hay and oat hay.

Corn (sweet) forage and stover
The product labels for all pertinent EC and 9.79 lb/gal RTU formulations must be modified as follows to reflect the parameters of use patterns for which adequate data are available for malathion preharvest use on sweet corn: (i) a maximum of five foliar applications per growing season of the 5 lb/gal EC formulation at 1.25 lb ai/A/application using ground equipment, with a 5-day retreatment interval and a 5-day PHI; and (ii) a maximum of five foliar applications per growing season of the 9.79 lb/gal RTU formulation at 0.61 lb ai/A/application using aerial ULV equipment, with a 5-day retreatment interval and a 5-day PHI.

Adequate field trial data have been submitted for sweet corn forage but not for sweet corn stover. The available data for field corn stover may not be translated to sweet corn stover because the proposed use patterns are not identical for both types of corn. Therefore, the following are required: Data depicting residues of malathion and malaoxon in/on sweet corn stover harvested 5 days following the last of: (i) five foliar applications per growing season of the 5 lb/gal EC formulation at 1.25 lb ai/A/application using ground equipment, with a 5-day retreatment interval; and (ii) five foliar applications per growing season of the 9.79 lb/gal RTU formulation at 0.61 lb ai/A/application using aerial ULV equipment, with a 5-day retreatment interval. The number of field trials and geographic locations of trial sites should be in compliance with the current guidance.

Sorghum forage and stover
The product labels for all pertinent EC and 9.79 lb/gal RTU formulations must be modified as follows to reflect the parameters of use patterns for which adequate data are available for malathion preharvest use on sorghum: (i) a maximum of three foliar applications per growing season of the 5 lb/gal EC formulation at 1.25 lb ai/A/application using ground equipment, with a 7-day retreatment interval and a 7-day PHI; and (ii) a maximum of three foliar applications per growing season of the 9.79 lb/gal RTU formulation at 0.61 lb ai/A/application using aerial ULV equipment, with a 7-day retreatment interval and a 7-day PHI.

The following are required: Data depicting residues of malathion and malaoxon in/on sorghum forage and stover harvested 7 days following the last of: (i) three foliar applications per growing season of the 5 lb/gal EC formulation at 1.25 lb ai/A/application using ground equipment, with a 7-day retreatment interval; and (ii) three foliar applications per growing season of the 9.79 lb/gal RTU formulation at 0.61 lb ai/A/application using aerial ULV equipment, with a 7-day retreatment interval. The number of field trials and geographic locations of trial sites should be in compliance with the current guidance.

Wheat forage, hay and straw.
The product label for all pertinent EC and 9.79 lb/gal RTU formulations must be modified as follows to reflect the parameters of use patterns for which adequate data are available for malathion preharvest use on wheat: (i) a maximum of three foliar applications per growing season of the 5 lb/gal EC formulation at 1.25 lb ai/A/application using ground equipment, with a 7-day retreatment interval and a 7-day PHI; and (ii) a maximum of three foliar applications per growing season of the 9.79 lb/gal RTU formulation at 0.61 lb ai/A/application using aerial ULV equipment, with a 7-day retreatment interval and a 7-day PHI.

Wheat forage, hay and straw.
Adequate field trial data have been submitted for wheat forage and straw, but not for wheat hay. Therefore, the following data are required: Data depicting residues of malathion and malaoxon in/on wheat hay harvested 7 days following the last of: (i) three foliar applications per growing season of the 5 lb/gal EC formulation at 1.25 lb ai/A/application using ground equipment, with a 7-day retreatment interval; and (ii) three foliar applications per growing season of the 9.79 lb/gal RTU formulation at 0.61 lb ai/A/application using aerial ULV equipment, with a 7-day retreatment interval. The number of field trials and geographic locations of trial sites should be in compliance with the current guidance.

Cotton, seed and gin byproducts
The product labels for all pertinent EC, 4.1 lb/gal RTU, and 9.79 lb/gal RTU formulations must be modified as follows to reflect the parameters of use patterns for which adequate data are available for malathion use on cotton: (i) 25 foliar applications, with 3-day retreatment intervals, of the 5 lb/gal EC formulation at 2.5 lb ai/A/application in 30 gal/A using ground equipment; (ii) 25 foliar applications, with 3-day retreatment intervals, of the 4.1 lb/gal RTU formulation at 1.15 lb ai/A/application using aerial ULV equipment; and (iii) 25 foliar applications, with 3-day retreatment intervals, of the 9.79 lb/gal RTU formulation at 1.22 lb ai/A/application using aerial ULV equipment. The available data will support a 0-day PHI.

Table 1 of OPPTS GLN 860.1000 recognizes cotton gin byproducts (commonly called gin trash) as a RAC of cotton; therefore, data depicting residues of malathion and malaoxon in/on cotton gin byproducts following applications of representative EC and RTU formulations according to the maximum proposed use patterns described above must be submitted. The number of field trials and geographic locations of trial sites should be in compliance with the current guidance.

Dates
Data have been submitted reflecting multiple applications of Dust formulations to Date trees. These data, which are under review, indicate that the present tolerance on dates will not be exceeded. The tolerance will be reassessed when it has been determined that adequate data have been submitted.

Processed Food/Feed: Barley, Oats, Rye
The required processing data for stored wheat grain resulting from postharvest applications may be translated to processed commodities of barley, oats, and rye.

Processed Food/Feed: Wheat
A processing study is required depicting the potential for concentration of residues of malathion and malaoxon in bran, flour, germ, middlings, and shorts processed from postharvest-treated wheat grain according to the same treatment schedule that was used in the submitted field corn and wheat grain studies.

Processed Food/Feed: Flax
A new flax processing study utilizing exaggerated application rate (5x) is required. If the exaggerated field trial should result in non-quantifiable residues in/on the RAC, then the harvested RAC samples need not be processed, and a tolerance for flax meal will not be required. If the exaggerated rate should produce quantifiable residues in/on the RAC, then the harvested RAC samples should be processed and malathion residues of concern should be measured in flax meal.

Water, Fish, and Irrigated Crops
Malathion remains registered for use on aquatic areas (including intermittently flooded areas, stagnant water, and temporary rain pools). The nature and magnitude of residues of malathion in drinking and irrigated water resulting from aquatic uses have not been delineated. Therefore, the data requirements imposed in the Malathion Reregistration Standard for these guideline topics remain outstanding. In lieu of the required residue data, the registrant(s) may modify malathion use to allow broadcast use only over intermittently flooded areas, and that applications may not be made around bodies of water where fish or shellfish are grown and/or harvested commercially.

Field Rotational Crops
The registrant had been requested to conduct limited field rotational crop studies. Rotational crop restrictions are needed on malathion end-use product labels. The appropriate plantback intervals will be determined pending submission of the required field rotational crop studies.

Occupational Exposure Data for OPPTS Guidelines

Dermal and inhalation risks could not be quantitatively assessed for four exposure scenarios because there are no appropriate chemical-specific or PHED data sets available. These scenarios are:

- (7) applying sprays with a helicopter (all crops)
- (9) applying dusts with a power duster; no PHED data exist.
- (10) dipping plants; no PHED data exist.
- (12) mixing/loading/appiying with a backpack sprayer; no PHED data exist for baseline.

Additional foliar dislodgeable residue data for crops other than turf are needed to further refine the non-cancer and cancer risk estimates for restricted entry intervals (REIs) for malathion.

These scenarios are of concern given the results from the other scenarios assessed. However, HED defers data requirements until risk management decisions have been finalized.

Table 17: Occupational Handler Short-term and Intermediate-term Risks from Malathion at Baseline, with Additional PPE, and with Engineering Controls.

Exposure Scenario (Scenario #)	Crop Type or Target	Baseline			Personal Protective Equipment (PPE)[a]			Engineering Controls		
		Dermal MOE[b] (UF=100)	Inhalation MOE[c] (UF=1000)	Total Risk Index (ARI)[d]	Dermal MOE[b] (UF=100)	Inhalation MOE[c] (UF=1000)	Total Risk index (ARI)[d]	Dermal MOE[b] (UF=100)	Inhalation MOE[c] (UF=1000)	Total Risk Index (ARI)[d]
Mixer/Loader Exposure										
Mixing/Loading Liquids for Groundboom Application (1a)	ag (pumpkins)	7.5	9,400	0.08	950 GO	9,400 NR	4.7	N/A		
	ag (veg)	30	38,000	0.3	3,800 GO	38,000 NR	19			
	golf course turf	3.5	4,300	0.03	440 GO	4,300 NR	2.2			
	sod farm	1.7	2,200	0.02	220 GO	2,200 NR	1.1			
	ornamentals	46	58,000	0.5	5,900 GO	58,000 NR	29			
Mixing/Loading Liquids for Aerial and Chemigation Application (1b)	ag (fruit & nut)	0.6	720	0.01	98	3,600	0.8	190	10,000	1.6
	ag (pumpkin)	1.7	2,200	0.02	290	2,200 NR	1.2	N/A		
	ag (veg)	6.9	8,600	0.07	1,200	8,600 NR	5			
	turf	0.4	490	0.004	68	2,500	0.5	135	7,200	1.1
	pine trees	1.3	1,700	0.01	230	8,300	1.8	N/A		
	mosquitoes	1.6	2,000	0.02	280	2,000 NR	1.2			
	ULV ag crops	1.3	1,500	0.01	220	7,800	1.7			
	ULV mosquitoes	0.07	860	0.007	120	4,400	0.94	240	12,900	2.0
Mixing/Loading Liquids for Airblast Sprayer (1c)	ag (fruit & nut)	5.0	6,300	0.04	860	6,300 NR	3.7	N/A		
	ag (citrus fruit)	15	19,000	0.15	190 GO	19,000 NR	1.7			
	ornamentals	12	14,000	0.12	150 GO	1,400 NR	1.4			
Mixing/Loading Liquids for Dipping (1d)	grape root dip	640	790,000	6.3	N/A	N/A	N/A	N/A		
Mixing/Loading Liquids for a Fogger (1e)	thermal fogger (mosquitoes)	15	18,000	0.15	1,900 GO	18,000 NR	10	N/A		
	non-thermal fogger (mosquitoes)	7.6	9,500	0.08	960 GO	9,500 NR	5			
Mixing/Loading Liquids for Handgun (1f)	turf	28	35,000	0.28	3,500 GO	35,000 NR	17	N/A		
Mixing/Loading Dusts for Power Duster or Direct Application (2)	stored grain facility	530	23,000	4.4	N/A					

Table 17: Occupational Handler Short-term and Intermediate-term Risks from Malathion at Baseline, with Additional PPE, and with Engineering Controls.

Exposure Scenario (Scenario #)	Crop Type or Target	Baseline			Personal Protective Equipment (PPE)[a]			Engineering Controls		
		Dermal MOE[b] (UF=100)	Inhalation MOE[c] (UF=1000)	Total Risk Index (ARI)[d]	Dermal MOE[b] (UF=100)	Inhalation MOE[c] (UF=1000)	Total Risk index (ARI)[d]	Dermal MOE[b] (UF=100)	Inhalation MOE[c] (UF=1000)	Total Risk Index (ARI)[d]
Mixing/Loading Wettable Powders for Groundboom Application (3a)	berries	3	130	0.02	85	660	0.4	1,100	24,000	8
Mixing/Loading Wettable Powders for Aerial Application (3b)	berries	0.68	30	0.01	19	150	0.08	260	5,400	1.7
Mixing/Loading Wettable Powders for Airblast Sprayer (3c)	berries	5.9	260	0.21	170	1,300	0.7	2,500	52,000	4
Applicator Exposure										
Applying Sprays with an Airblast Sprayer (4)	ag (fruit & nut)	41	1,700	0.33	67	8,400	0.6	100	17,000	0.94
	berries	61	2,500	0.50	100	13,000	0.93	160	26,000	1.5
	ag (citrus fruit)	120	5,000	1.0	N/A					
	ornamentals	93	3,900	0.84	150	19,000	1.4	N/A		
Applying Sprays with a Groundboom Sprayer (5)	berries	780	7,600	4.0	N/A					
	ag (pumpkins)	1,600	15,000	7.7						
	ag (veg)	6,300	61,000	31						
	ornamentals	9,600	94,000	48						
	golf course turf	720	7,000	3.6						
	sod farm	360	3,500	1.8						
Applying Sprays with a Fixed-Wing Aircraft (liquid formulations) (6)	ag (fruit& nut)	See Eng. Controls						330	13,000	3
	berries	See Eng. Controls						500	18,000	4
	ag (pumpkins)	See Eng. Controls						1,000	38,000	8
	ag (veg)	See Eng. Controls						4,000	150,000	25
	pine trees	See Eng. Controls						770	29,000	6
	turf	See Eng. Controls						230	8,600	1.8
	mosquitoes	See Eng. Controls						930	35,000	7
	ULV ag crops	See Eng. Controls						730	28,000	6
	ULV mosquitoes	See Eng. Controls						420	15,200	3.3

Table 17: Occupational Handler Short-term and Intermediate-term Risks from Malathion at Baseline, with Additional PPE, and with Engineering Controls.

Exposure Scenario (Scenario #)	Crop Type or Target	Baseline			Personal Protective Equipment (PPE)[a]			Engineering Controls		
		Dermal MOE[b] (UF=100)	Inhalation MOE[c] (UF=1000)	Total Risk Index (ARI)[d]	Dermal MOE[b] (UF=100)	Inhalation MOE[c] (UF=1000)	Total Risk index (ARI)[d]	Dermal MOE[b] (UF=100)	Inhalation MOE[c] (UF=1000)	Total Risk Index (ARI)[d]
Applying Sprays with a Helicopter (liquid formulations) (7)	ag (fruit& nut), berries, ag (pumpkins), ag (veg), pine trees, turf, mosquitoes, ULV ag crops, ULV mosquitoes	No Adequate Data								
Applying Sprays with a Fogger (8)	thermal fogger (mosquitoes)	120	4,900	1.0	N/A					
	non-thermal fogger (mosquitoes)	61	2,500	0.5	100	13,000	0.93	160	26,000	1.5
Applying Dusts with a Power Duster (9)	stored grain facility	No Adequate Data								
Dipping Plants (10)	grape root dip	No Adequate Data								
Applying with a Handgun (turf) Sprayer (11)	turf	see PPE	see PPE	see PPE	120 GO	30,000 NR	1.2	N/A		
Mixer/Loader Applicator Exposure										
Mixing/Loading/Applying with a Low Pressure Handwand (12)	stored grain facility	3.5	6,000	0.03	810 GO	6,000 NR	3.4	N/A		
	agricultural premises	3.2	5,600	0.03	750 GO	5,600 NR	3.3			
	ornamentals	2.7	4,600	0.03	630 GO	4,600 NR	2.5			
	turf	4.2	7,000	0.04	1,000 GO	7,000 NR	4.2			
Mixing/Loading/Applying with a Backpack Sprayer (13)	grain	See PPE.	See PPE.	See PPE.	140 GO	6,000 NR	1.1	N/A		
	agricultural premises				130 GO	5,600 NR	1.0			
	ornamentals				170	4,600 NR	1.2			
	turf				1,600 GO	7,000 NR	1.3			
Mixing/Loading/Applying with a Hose End Sprayer (14)	mushrooms	320	5.4E+05	3.2	N/A					

Table 17: Occupational Handler Short-term and Intermediate-term Risks from Malathion at Baseline, with Additional PPE, and with Engineering Controls.

Exposure Scenario (Scenario #)	Crop Type or Target	Baseline			Personal Protective Equipment (PPE)[a]			Engineering Controls		
		Dermal MOE[b] (UF=100)	Inhalation MOE[c] (UF=1000)	Total Risk Index (ARI)[d]	Dermal MOE[b] (UF=100)	Inhalation MOE[c] (UF=1000)	Total Risk index (ARI)[d]	Dermal MOE[b] (UF=100)	Inhalation MOE[c] (UF=1000)	Total Risk Index (ARI)[d]
Mixing/Loading/Applying with a Paintbrush(15)	mosquitoes	39	13,000	0.37	294 GO	13,000 NR	2.3	N/A		
Flagger Exposure										
Flagging for Aerial Spray Applications (16)	ag (fruit & nut)	150	2,500	0.94	169	12,300	1.4	N/A	N/A	N/A
	berries	230	3,700	1.4	N/A					
	ag (pumpkin)	450	7,400	2.8						
	ag (veg)	1,800	29,000	13						
	pine trees	350	5,700	2.2						
	turf	100	1,700	0.63	100	8,500	0.89	230	86,000	2.2
	mosquitoes	420	6,900	2.6	N/A					
	ULV ag crops	330	5,400	2.0						
	ULV mosquitoes	185	3,000	1.2	N/A					

Footnotes:

[a] Personal Protective Equipment: Except where noted [GO = Gloves Only; NR = No Respirator], additional PPE means double layer of clothing, chemical resistant gloves, and dust/mist respirator.

[b] Dermal MOE (short- and intermediate-term) = NOAEL (50 mg/kg/day)/Daily Dermal Dose (mg/kg/day).

[c] Inhalation MOE(short- and intermediate-term) = LOAEL (25.8 mg/kg/day)/ Daily Inhalation Dose (mg/kg/day).

[d] Total ARI (short- and Intermediate-term) = 1 / ((1/Calculated Dermal MOE/Target Dermal MOE (100)) + (1 /Calculated Inhalation MOE/Target Inhalation MOE (1000))).

NF Not Feasible.

NA Not Applicable, because previous level of mitigation resulted in an ARI of >1.

Table 18: Occupational Combined Dermal and Inhalation Cancer Risk Assessment for Malathion at Baseline, with PPE, and with Engineering Controls.

Exposure Scenario (Scenario #)	Range of Application Rates[c] (lb ai/acre)	Crop Type or Target[d]	Area Treated or Amount Handled per Day[e]	Number of Exposures per Year	Baseline Total Cancer Risk	PPE Total Cancer Risk	Eng. Total Cancer Risk
Mixer/Loader Exposure							
Mixing/Loading Liquids for Groundboom Application (1a)	2	ag (pumpkins)[2]	80 acres	80	1.10e-04	1.34e-06	N/A
	0.5	ag (veg)[3]		80	2.88e-05	3.34e-07	N/A
	8.7	golf course turf[4]	40 acres	80	2.40e-04	2.84e-06	N/A
	8.7	sod farms[4]	80 acres	80	4.80e-04	5.85e-06	N/A
	2.6	ornamentals[5]	10 acres	80	1.80e-05	1.67e-07	N/A
Mixing/Loading Liquids for Aerial and Chemigation Application (1b)	6	ag (fruit & nut)[1]	350 acres	80	1.46e-03	9.72e-06	N/A
	2	ag med[2]		80	4.80e-04	4.85e-06	N/A
	0.5	ag low[3]		80	1.22e-04	1.22e-06	N/A
	8.7	turf[4]		80	2.10e-03	1.41e-05	5.24e-06
	2.6	pine trees[5]		80	6.24e-04	4.22e-06	N/A
	0.5	mosquitoes[6]	1,500 acres	80	5.22e-04	5.02e-06	N/A
	1.2	ULV ag crops[7]	800 acres	40	3.04e-04	2.50e-06	N/A
	0.23	ULV mosquitoes[8]	7,500 acres	80	1.22e-03	7.98e-06	2.97e-06
Mixing/Loading Liquids for Airblast Sprayer (1c)	6	ag (fruit & nut)[1]	40 acres	80	1.68e-04	1.66e-06	N/A
	2	ag (citrus fruit)[2]		80	5.52e-05	6.69e-07	N/A
	2.6	ornamentals[5]		80	7.19e-05	8.69e-07	N/A
Mixing/Loading Liquids for Dipping (1d)	1.9 lbai/100 gal.	grape root dip[10]	100 gal	80	1.32e-06	N/A	N/A
Mixing/Loading Liquids for a Fogger (truck) (1e)	0.51 lb ai/gal	thermal fogger[8] (mosquitoes)	160 gal	50	3.12e-05	4.13e-07	N/A
	9.9 lb ai/gal	non-thermal fogger[8] (mosquitoes)	16 gal	50	7.24e-05	8.17e-07	N/A
Mixing/Loading Liquids for Handgun (1f)	8.7	turf[4]	5 acres	80	3.02e-05	3.63e-07	N/A
Loading Dusts for Power Duster of Direct Application (2)	0.3 lbs ai/ 1,000 sq. ft.	stored grain facility[11]	6,000 sq. ft.	80	1.78e-06	N/A	N/A
Mixing/Loading Wettable Powders for Groundboom Application (3a)	4	berries[9]	80 acres	80	3.20e-04	1.65e-05	9.34e-07

Table 18: Occupational Combined Dermal and Inhalation Cancer Risk Assessment for Malathion at Baseline, with PPE, and with Engineering Controls.

Exposure Scenario (Scenario #)	Range of Application Rates[c] (lb ai/acre)	Crop Type or Target[d]	Area Treated or Amount Handled per Day[e]	Number of Exposures per Year	Baseline Total Cancer Risk	PPE Total Cancer Risk	Eng. Total Cancer Risk
Mixing/Loading Wettable Powders for Aerial Application (3b)	4	berries[9]	350 acres	80	1.39e-03	7.21e-05	4.08e-06
Mixing/Loading Wettable Powders for Airblast Sprayer (3c)	4	berries[9]	40 acres	80	1.57e-04	8.26e-06	N/A
Applicator Exposure							
Applying Sprays with an Airblast Sprayer (4)	6	ag (fruit & nut)[1]	40 acres	80	2.32e-05	1.31e-05	6.64e-07
	4	berries[9]		80	1.56e-05	8.69e-06	N/A
	2	ag (citrus fruit)[2]		80	7.79e-06	N/A	N/A
	2.6	ornamentals[5]		80	1.00e-05	5.69e-06	N/A
Applying Sprays with a Groundboom Sprayer (5)	4	berries[9]	80 acres	80	1.65e-06	N/A	N/A
	2	ag (pumpkins)[2]		80	7.60e-07	N/A	N/A
	0.5	ag (veg)[3]		80	1.67e-07	N/A	N/A
	2.6	ornamentals[5]	10 acres	80	1.67e-07	N/A	N/A
	8.7	golf course turf[4]	40 acres	80	1.67e-06	N/A	N/A
	8.7	sod farms[4]	80 acres	80	3.56e-06	N/A	N/A
Applying Sprays with a Fixed-Wing Aircraft (6)	6	ag (fruit & nut)[2]	350 acres	80	See Eng. Controls	See Eng. Controls	2.85e-06
	4	berries[9]	350 acres	80	See Eng. Controls	See Eng. Controls	1.90e-06
	2	ag (pumpkins)[2]	350 acres	80	See Eng. Controls	See Eng. Controls	9.51e-07
	0.5	ag (veg)[3]	350 acres	80	See Eng. Controls	See Eng. Controls	2.38e-07
	2.6	pine trees[5]	350 acres	80	See Eng. Controls	See Eng. Controls	4.13e-06
	8.7	turf[4]	350 acres	80	See Eng. Controls	See Eng. Controls	1.23e-06
	0.5	mosquitoes[6]	1,500 acres	80	See Eng. Controls	See Eng. Controls	1.02e-06
	1.2	ULV ag crops[7]	800 acres	80	See Eng. Controls	See Eng. Controls	1.30e-06

Table 18: Occupational Combined Dermal and Inhalation Cancer Risk Assessment for Malathion at Baseline, with PPE, and with Engineering Controls.

Exposure Scenario (Scenario #)	Range of Application Rates[c] (lb ai/acre)	Crop Type or Target[d]	Area Treated or Amount Handled per Day[e]	Number of Exposures per Year	Baseline Total Cancer Risk	PPE Total Cancer Risk	Eng. Total Cancer Risk
	0.23	ULV mosquitoes[8]	7,500 acres	80	See Eng. Controls	See Eng. Controls	2.35e-06
Applying Sprays with a Helicopter (7)	6	ag (fruit & nut)[2]	350 acres	80	No Acceptable Data	No Acceptable Data	No Acceptable Data
	4	berries[9]					
	2	ag (pumpkins)[2]					
	0.5	ag (veg)[3]					
	2.6	pine trees[5]					
	8.7	turf[4]					
	0.5	mosquitoes[6]	1,500 acres				
	1.2	ULV ag crops[7]	800 acres				
	0.5	ULV mosquitoes[8]	7,500 acres				
Applying Sprays with a Fogger (8)	0.51 lb ai/gal	thermal fogger[8] (mosquitoes)	160 gal	50	5.17e-06	N/A	N/A
	9.9 lb ai/gal	non-thermal fogger[8] (mosquitoes)	16 gal	50	1.03e-05	5.38e-06	N/A
Applying Dusts with a Power Duster (9)	0.3 lb ai/1,000 sq. ft.	stored grain facility[11]	6,000 sq. ft.	No Data	No Data	No Data	No Data
Dipping Plants (10)	1.9 lb ai/100 gal	grape dip[11]	100 gal	No Data	No Data	No Data	No Data
Applying with a Handgun (11)	8.7	turf[4]	5 acres	80	3.73e-06	N/A	N/A
Mixer/Loader/Applicator Exposure							
Mixing/Loading/Applying Liquid with a Low Pressure Handwand (12)	0.25 lb ai/gal	stored grain facility[11]	40 gal	80	2.40e-04	1.67e-06	N/A
	0.27 lb ai/gal	agricultural premises[12]	40 gal	80	2.64e-04	1.82e-06	N/A
	0.06 lb ai/gal	ornamentals[5]	40 gal	80	3.11e-04	4.56e-07	N/A
	8.7	turf[4]	1 acre	80	2.08e-04	1.06e-06	N/A
Mixing/Loading/Applying with a Backpack Sprayer (13)	0.25 lb ai/gal	stored grain facility[11]	40 gal	80	See PPE	6.68e-06	N/A

Table 18: Occupational Combined Dermal and Inhalation Cancer Risk Assessment for Malathion at Baseline, with PPE, and with Engineering Controls.

Exposure Scenario (Scenario #)	Range of Application Rates[c] (lb ai/acre)	Crop Type or Target[d]	Area Treated or Amount Handled per Day[e]	Number of Exposures per Year	Baseline Total Cancer Risk	PPE Total Cancer Risk	Eng. Total Cancer Risk
	0.27 lb ai/gal	agricultural premises[12]	40 gal	80	See PPE	7.19e-06	N/A
	0.06	ornamentals[5]	40 gal	80	See PPE	1.00e-06	N/A
	8.7	turf[4]	1 acre	80	See PPE	5.85e-06	N/A
Mixing/Loading/Applying with a Hose End Sprayer (14)	0.039 lb ai/1,000 sq. ft.	mushrooms[13]	9,000 sq. ft.	80	2.64e-06	N/A	N/A
Mixing/Loading/Applying with a Paintbrush (15)	0.1 lb ai/gal	mosquitoes[6]	5 gal	80	2.18e-05	3.20e-06	N/A
Flagger Exposure							
Flagging for Aerial Spray Applications (16)	6	ag (fruit & nut)[1]	350 acres	80	7.26e-06	N/A	N/A
	4	berries[9]		80	4.75e-06	N/A	N/A
	2	ag (pumpkins)[2]		80	2.44e-06	N/A	N/A
	0.5	ag (veg)[3]		80	6.00e-07	N/A	N/A
	2.6	pine trees[5]		80	3.15e-06	N/A	N/A
	8.7	turf[4]		80	1.06e-05	8.48e-06	N/A
	0.5	mosquitoes[6]	1,500 acres	80	2.60e-06	N/A	N/A
	1.2	ULV ag crops[7]	800 acres	40	1.52e-06	N/A	N/A
	0.23	ULV mosquitoes[8]	7,500 acres	80	6.02e-06	N/A	N/A

Footnotes:

a **Baseline** exposure represents long pants, long sleeved shirt, no gloves, and open mixing/loading; **PPE** exposure represents double layer of clothing or coveralls, chemical resistant gloves, and open mixing/loading; **engineering** exposure represents long pants, long sleeved shirt, no gloves, and closed mixing/loading. PHED Surrogate Exposure Guide - Draft. August 1998.

b **Baseline** inhalation exposure represents no respirator; **PPE** exposure represents a dust/mist respirator; **engineering controls** represents no respirator. PHED Surrogate Exposure Guide - Draft. August 1998.

c Application rates are based on maximum food tolerances suggested by EPA and maximum application rates listed on labels.

d Crop types or targets are selected as follows:

1 Based on maximum application rates from residue field trials in support of food tolerances for pecans, apples, and pineapples.
2 Based on maximum application rates from residue field trials in support of food tolerances for pumpkins, melon, eggplant (groundboom & aerial) and cherries, citrus fruits, and peaches (airblast)
3 Based on maximum application rates from residue field trials in support of food tolerances for various vegetable crops.
4 Based on labeled maximum rates for turf, including golf course turf, sod farms and lawns of residences, businesses and parks. (EPA Reg. 655-777, 769-621 and 909-101).
5 Based on labeled maximum rates for ornamentals and pine trees (EPA Reg. 655-77, 67760-1 and 5905-196).
6 Based on labeled maximum rates for mosquitoes including standing water (based on residue field trials) and terrestrial uses (EPA Reg. 34704-108).
7 Based on labeled maximum rates for ULV-type agricultural crops (e.g., corn, wheat, and grain). (EPA Reg. 4787-8)
8 Based on labeled maximum rates for mosquitoes applications for ULV-type (EPA Reg. 4787-8).
9 Based on maximum application rates from residue field trials in support of food tolerances for berries.
10 Based on maximum application rates from residue field trials in support of food tolerances for grape root dip.

11 Based on maximum application rates from residue field trials in support of food tolerances for stored grain.
12 Based on maximum application rates from residue field trials in support of food tolerances for poultry premises and agricultural premises used as a bait spray.
13 Based on maximum application rates from residue field trials in support of food tolerances for mushrooms.

e Amount handled per day are from EPA estimates of acres treated, gallons applied, or square feet treated.

f Daily Dermal Exposure (mg/day) = Dermal Unit Exposure (mg/lb ai) x Application Rates (lb ai/acre; lb/gal; and ai/sq ft) x Amount Handled per day (acres, gallons, sq. ft.).

g Daily Inhalation Exposure (mg/day) = Inhalation Unit Exposure (μg/lb ai) x (1 mg/1,000 μg) Conversion x Application rate (lb ai/acre; lb/gal; and ai/sq ft) x Amount Handled per day (acres, gallons, sq. ft.)

h Mixing/loading wettable powders is applied as a "surrogate" to mixing/loading dusts.

i Applying sprays with a fogger uses "surrogate" PHED data for applying sprays with an airblast sprayer.

Baseline Total Daily Dose = [Baseline Daily Dermal Exposure (mg/day) * 0.10 (Dermal Absorption Factor) + Baseline Daily Inhalation Exposure (mg/day)]/body weight (70 kg).

Number of exposures per year is based on maximum number of applications supported by residue field trial data.

Baseline LADD (mg/kg/day) = Baseline Total Daily Dose (mg/kg/day) * (Number of days exposure per year/365 days per year) * 35 years worked/70 year lifetime.

Baseline Total Cancer Risk = Baseline LADD (mg/kg/day) * (Q1*), where Q1* = 1.52×10^{-3} (mg/kg/day).

NF Not Feasible.

Table 19: Residential Handler Short-term and Cancer Risks to Malathion at Baseline.

Exposure Scenario (Scen. #)	Crop Type or Target	Maximum Application Rates (lb ai/A)	Amount Handled per Day	Baseline Dermal MOE[c] (UF=100)	Baseline Inhalation MOE[d] (UF=1000)	Baseline Total Aggregate Risk Index (ARI)[e]	Baseline Total Daily Dose (mg/kg/day)	LADD[f] (mg/kg/day)	Baseline Cancer Risk[g]
Mixer/Loader/Applicator Exposure									
Mixing/Loading/Applying Liquid with a Low Pressure Handwand (1a)	Fruit Trees	0.034 lb ai/ gal	5 gal	206	350,000	2.1	0.02	2.40e-05	3.70e-08
	Ornamentals	0.034 lb ai/gal	5 gal	206	350,000	2.1	0.02	2.40e-05	3.70e-08
	Turf	0.18 lb ai/1000 sq. ft	1,000 ft^2	190	350,000	1.9	0.03	2.60e-05	4.00e-08
	Vegetable/Small Fruit Garden	0.023 ai lb/gal	5 gal	304	660,000	3.0	0.02	1.60e-05	2.40e-08
	Mosquitoes (household pests)	0.1547 lb ai/gal	5 gal	45	530,000	0.5	0.11	1.11e-04	1.69e-07
Mixing/Loading/Applying Wettable Powder with a Low Pressure Handwand (1b)	Fruit Trees	0.010 lb ai/gal	5 gal	278	33,000	2.6	0.02	1.88e-05	2.90e-08
	Ornamentals	0.015 lb ai/gal	5 gal	185	22,000	1.7	0.03	2.82e-05	4.30e-08
	Vegetable/Small Fruit Garden	0.018 lb ai/gal	5 gal	156	18,000	1.4	0.03	3.34e-05	5.10e-08
Mixing/Loading/Applying Liquids with a Hose End Sprayer (2)	Fruit Trees	0.034 lb ai/gal	50 gal	69	110,000	0.7	0.08	7.53e-05	1.14e-07
	Ornamentals	0.034 lb ai/gal	50 gal	69	110,000	0.7	0.08	7.53e-05	1.14e-07
	Turf	0.18 lb ai/1000 sq. ft	1,000 ft^2	625	1,290,000	6.3	0.01	8.02e-06	1.20e-08
	Vegetable/Small Fruit Garden	0.023 lb ai/gal	50 gal	101	220,000	0.99	0.05	4.92e-05	7.50e-08
	Mosquitoes (household pests)	0.1547 lb ai/gal	50 gal	15	160,000	0.02	0.33	3.33e-04	5.06e-07

Table 19: Residential Handler Short-term and Cancer Risks to Malathion at Baseline.

Exposure Scenario (Scen. #)	Crop Type or Target	Maximum Application Rates (lb ai/A)	Amount Handled per Day	Baseline Dermal MOE[c] (UF=100)	Baseline Inhalation MOE[d] (UF=1000)	Baseline Total Aggregate Risk Index (ARI)[e]	Baseline Total Daily Dose (mg/kg/day)	LADD[f] (mg/kg/day)	Baseline Cancer Risk[g]
Mixing/Loading/Applying Liquids with a Backpack Sprayer (3)	Fruit Tree	0.034 lb ai/gal	5 gal	5000	350,000	50	0.001	1.07e-06	2.00e-09
	Ornamentals	0.034 lb ai/gal	5 gal	5000	350,000	50	0.001	1.07e-06	2.00e-09
	Turf	0.18 lb ai/1000 sq. ft	1,000 ft^2	5000	350,000	50	0.001	1.07e-06	2.00e-09
	Vegetable/Small Fruit Garden	0.023 lb ai/gal	5 gal	5000	650,000	50	0.001	1.04e-06	2.00e-09
	Mosquitoes (household pests)	0.1547 lb ai/gal	5 gal	887	530,000	9	0.006	6.33e-06	1.00e-08
Mixing/Loading/Applying Liquids with a Fogger (4) Note[1]	Mosquitoes	0.152 lb ai/gal	5 gal	Note[1]	Note[1]	Note[1]	Note[1]	Note[1]	Note[1]
Mixing/Loading/Applying Dust using a Shaker Can (5) Note[2]	Ornamentals	2 lb ai/A	1000 ft^2	2	Note[2]	Note[2]	3.0	0.03	4.56e-05
	Turf	0.10 lb ai/1000 sq. ft	1000 ft^2	<1			6.5	0.065	9.88e-05
	Vegetable/Small Fruit Garden	2.5 lb ai/A	1000 ft^2	1			3.7	0.037	5.62e-05

Footnotes:

a Baseline Dermal Dose (mg/kg/day) = Daily Dermal Exposure (mg/day) / Body Weight (70 kg).
b Baseline Inhalation Dose (mg/kg/day) = Daily Inhalation Exposure (mg/day) / Body Weight (70 kg).
c Baseline Dermal MOE = NOAEL (50 mg/kg/day) / Baseline Dermal Dose (mg/kg/day).
d Baseline Inhalation MOE = LOAEL (25.8 mg/kg/day) / Baseline Inhalation Dose (mg/kg/day).
e Total ARI (short- and Intermediate-term) = 1 / ((1/Calculated Dermal MOE/Target Dermal MOE (100)) + (1/Calculated Inhalation MOE/Target Inhalation MOE (1000))).
f Baseline Total Daily Dose (mg/kg/day) = [Baseline Daily Dermal Exposure (mg/day) * 0.10 (Dermal Absorption Factor) + Baseline Daily Inhalation Exposure (mg/day)]/body weight (70 kg).
g Lifetime Average Daily Dose, LADD (mg/kg/day) = Baseline Total Daily Dose (mg/kg/day) * (5 days exposure per year/365 days per year) * (50 years/70 year lifetime).
h Cancer Risk = LADD (mg/kg/day) * (Q1*), where Q1* = 1.52 x 10^{-3} (mg/kg/day).

Note[1] No PHED data are available for this scenario. However, it is believed that the scenario for mixing/loading and applying liquid for backpack sprayer application to control mosquitoes serves as a comparable, if not worst case, surrogate for the use of a small fogger unit (based on EPAReg. No. 769-844).

Note[2] No PHED data are available for this scenario. Draft SOPs for Residential Exposure Assessment (December 1997) include an assumption that the residential handler is exposed (dermal and inhalation) to 10% of the active ingredient applied by shaker can. When this assumption is used for only the dermal endpoint, the resulting MOEs are sufficiently low as to not warrant further analyses.

Table 20: Residential Short- and Intermediate-Term Postapplication Scenarios and Estimated Risks for Malathion

Scenario	Crop or Target	Receptor	Application Rate Per Treatment (AR) (lbs ai/sq ft)[a]	DFR (ug/cm^2)[b]	Grt (ug/cm^2)[c]	Srt (ug/g)[d]	Transfer Coefficient (Tc) (cm^2/hr)	Exposure Time (ET) (hrs/day	Dermal Abs. (%)	Surface Area (SA) (cm^2/ event)	Freq. (FQ) (events/ hr)	IgR (cm^2/day) or (mg/day)[e]	BW (kg)	ADD (mg/kg/ day)[f]	MOE[g]
Dermal exposure	Turf (handgun) Commercial	Adult	0.00019	1.2	-	-	43,000			-	-	-	70	1.4	34
		Toddler					8,700						15	1.32	36
	Turf (air ULV)	Adult	0.0000053	0.012			43,000	2	100				70	0.015	3400
		Toddler					8,700						15	0.014	3600
	Turf (grnd ULV)	Adult	0.0000025	0.0008			43,000						70	0.001	50000
		Toddler					8,700						15	0.001	50000
	Vegetable/Small Fruit Gardens	Adult	0.000115	11.2	-	-	10,000	0.67	100	-	-	-	70	1.07	47
	"Pick-your-own" strawberries	Adult	0.000115	11.2			10,000	1	100				70	1.6	31
	Fruit Trees & Ornamentals	Adult	0.000085	8.3	-	-	10,000	0.67	100	-	-	-	70	0.79	63
Hand-to-Mouth	Turf (handgun) Commercial	Toddler	0.000 9	1.2	-	-	-	2	-	350	1.56	-	15	0.09	600
	Turf (air ULV)		0.0000053	0.012										0.0008	57000
	Turf (grnd ULV)		0.0000025	0										0.00005	860000
Turfgrass ingestion	Turf (handgun) Commercial	Toddler	0.00019	-	1.2	-	-	-	-	-	-	25	15	0.002	25000
	Turf (air ULV)		0.0000053		0.012									2.0e-05	2.5e+06
	Turf (grnd ULV)		0.0000025		0.008									1.3e-05	3.8e+06

Table 20: Residential Short- and Intermediate-Term Postapplication Scenarios and Estimated Risks for Malathion

Scenario	Crop or Target	Receptor	Application Rate Per Treatment (AR) (lbs ai/sq ft)[a]	DFR (ug/cm^2)[b]	Grt (ug/cm^2)[c]	Srt (ug/g)[d]	Transfer Coefficient (Tc) (cm^2/hr)	Exposure Time (ET) (hrs/day	Dermal Abs. (%)	Surface Area (SA) (cm^2/ event)	Freq. (FQ) (events/ hr)	IgR (cm^2/day) or (mg/day)[e]	BW (kg)	ADD (mg/kg/ day)[f]	MOE[g]
Incidental soil ingestion	Turf (handgun) Commercial	Toddler	0.00019	-	-	62	-	-	-	-	-	100	15	0.0004	125000
	Turf (air ULV)		0.0000053			0.6								4.0e-06	1.3e+07
	Turf (grnd ULV)		0.0000025			0.04								3.0e-07	1.7e+08
	Vegetable/ Small Fruit Gardens	Toddler	0.000115	-	-	38	-	-	-	-	-	100	15	0.0003	170000

Footnotes:

a Application rates are estimated as follows: turf(handgun) - 0.18 lb ai per 1,000 sq. ft.; turf (air ULV) - (0.23 lb ai/A)/43,560 sq. ft. per A; turf (ground ULV) - (0.11 lb ai/A)/43,560 sq. ft. per A; vegetable/small fruit gardens- (0.023 lb ai/gal * 5 gallons)/1,000 ft^2; fruit trees and ornamentals-(0.034 lb ai/gal * 5 gal)/2,000 ft^2

b Dislodgeable foliar residue (ug/cm^2) = [AR (lbs ai/ft^2) * fraction ai retained on foliage (1.3% [* 0.35 for air ULV, or * 0.05 for ground ULV]) * 4.54E+8 ug/lb * 1.08E-3 ft^2/cm^2].

c Grass residue (ug/cm^2) = [AR (lbs ai/ft^2) * fraction ai retained on foliage (1.3% [* 0.35 for air ULV, or * 0.05 for ground ULV]) * 4.54E+8 ug/lb * 1.08E-3 ft^2/cm^2].

d Soil residue (ug/cm^2) = [AR (lbs ai/ft^2) [* 0.35 for air ULV, or * 0.05 for ground ULV] * 4.54E+8 ug/lb * 1.08E-3 ft^2/cm^2 * 0.67 cm^3/g soil].

e Ingestion rate: cm^2/day for grass ingestion, and mg/day for incidental soil ingestion.

f Average daily dose (ADD) (mg/kg/day)

Dermal exposure: = [DFR (ug/cm^2) * Tc (cm^2/hr) * mg/1,000 ug * ET (hrs/day) * absorption factor (1.0)] / [BW (kg)];

Hand-to-mouth: = [DFR (ug/cm^2) * SA (cm^2/event) * FQ (events/hr) * mg/1,000 ug * ET (hrs/day)] / [BW (kg)];

Turfgrass ingestion: = [GRt (ug/cm^2) * IgR (cm^2/day) * mg/1,000 ug] / [BW (kg)]; and

Incidental soil ingestion: = [SRt (ug/g) * IgR (mg/day) * g/1,000,000 ug] / [BW (kg)].

g MOE = NOAEL (50 mg/kg/day) / ADD.

Table 21: Residential Postapplication Scenarios and Estimated Cancer Risks for Malathion

Scenario	Crop or Target	Application Rate (lbs ai/sq ft)	DFR (ug/cm^2)	Exposure Time (hr./day)[a]	Tc (cm^2/hr)[b]	BW (kg)	LADD[c]	Cancer Risk[d]
Dermal exposure	Turf (handgun)	0.00019	1.2	2	43,000	70	0.0014	2.1e-06
	Turf (air ULV)	0.0000053	0.012				0.000015	2.3e-08
	Turf (ground ULV)	0.0000025	0.0008				0.000001	1.5e-09
	Vegetable/ Small Fruit Gardens	0.000115	11.2	0.67	10,000		0.0011	1.6e-06
	"Pick-your-own" strawberries	0.000115	11.2	1	10,000		0.0016	2.4e-06
	Fruit Trees & Ornamentals	0.000085	8.3	0.67	10,000		0.00005	7.6e-08

Footnotes:

[a] Exposure time used is same as for short-term exposure estimates and is, therefore conservative for cancer risk estimates.
[b] Transfer coefficients are same as for short-term exposure estimates and are, therefore conservative for cancer risk estimates.
[c] LADD (mg/kg/day) = Dermal Dose (mg/kg/day) * (10% dermal absorption factor) * (5 days exposure /365 days per year) * (50 years exposure/70 year lifetime).
[d] Cancer Risk = LADD (mg/kg/day) * (Q1*), where Q1* = 1.52×10^{-3} (mg/kg/day).

Table 22: Non-occupational Scenarios for Use in Aggregate Exposure Assessments.

Scenario	Application Rate	Crop Type or Target	Dermal Daily Dose (mg/kg/day)	Dermal MOE (UF=100)	Inhalation Daily Dose (mg/kg/day)	Inhal. MOE (UF=1000)	Total Aggregate Risk Index (ARI)	LADD (mg/kg/day)	Cancer Risk
Adult Aggregate Scenarios									
M/L/A Liquids with a Low Pressure Handwand	0.034 (lb ai/gal)	Ornamentals or Fruit Trees	0.24	206	0.00007	350,000	2	3.78e-05	5.75e-08
Postapplication Inhalation and Dermal Contact with Turf Following Ground ULV Truck Fogger Application	0.0000025 (lb ai/sq ft)	Public Mosquito Control	0.001	50000	0.001	26,000	25	0.000015	2.3e-08
Toddler Aggregate Scenarios									
Postapplication Hand-to-mouth from Turf Following Ground ULV Truck Fogger Application	0.0000025 (lb ai/sq ft)	Public Mosquito Control	0.0008	57,000	Note [1]	Note[1]	Note[1]	Note[2]	Note[2]
Postapplication Inhalation and Dermal Contact with Turf Following Ground ULV Truck Fogger Application	0.0000025 (lb ai/sq ft)	Public Mosquito Control	0.001	50000	0.003	8600	8	Note[2]	Note[2]

Note [1] Not applicable because inhalation is aggregated already with dermal contact scenario

Note[2] No toddler cancer methodology presently.

DP BARCODE: D255364 REREG CASE # 0248

CASE: 818961 DATA PACKAGE RECORD DATE: 12/03/99
SUBMISSION: S529758 BEAN SHEET Page 1 of 1

* * * CASE/SUBMISSION INFORMATION * * *

CASE TYPE: REREGISTRATION ACTION: 623 INITIATE RED CHAPTER
CHEMICALS: 057701 Malathion (ANSI) 100.00 %

ID#: 057701
COMPANY:
PRODUCT MANAGER: 53 BETTY SHACKLEFORD ROOM: CS1
PM TEAM REVIEWER: PATRICIA MOE 703-308-8011 ROOM: CM2 675
RECEIVED DATE: 09/10/97 DUE OUT DATE: 12/09/97

* * * DATA PACKAGE INFORMATION * * *

DP BARCODE: 255364 EXPEDITE: N DATE SENT: 04/20/99 DATE RET.: 11/08/99
CHEMICAL: 057701 Malathion (ANSI)
DP TYPE: 999 Miscellaneous Data Package
CSF: N LABEL: N

ASSIGNED TO	DATE IN	DATE OUT
DIV : HED	04/20/99	11/08/99
BRAN: RRB2	04/20/99	11/08/99
SECT: IO	04/20/99	11/08/99
REVR : PDESCHAM	04/20/99	11/08/99
CONTR:	/ /	/ /

ADMIN DUE DATE: 07/15/99
NEGOT DATE: / /
PROJ DATE: / /

* * * DATA REVIEW INSTRUCTIONS * * *

SRRD has requested that HED provide a Preliminary risk assessment on malathion for Registrant Error-only review.

* * * DATA PACKAGE EVALUATION * * *

No evaluation is written for this data package

* * * ADDITIONAL DATA PACKAGES FOR THIS SUBMISSION * * *

DP BC	BRANCH/SECTION	DATE OUT	DUE BACK	INS	CSF	LABEL
238903	ERB1/IO	09/10/97	12/09/97	Y	N	N
238904	ERB1/IO	09/10/97	12/09/97	Y	N	N
238906	ERB1/IO	09/10/97	12/09/97	Y	N	N
238907	RRB2/IO	09/10/97	12/09/97	Y	N	N
239439	RAB3/IO	09/18/97	12/27/97	Y	N	N
247492	RRB4/IO	07/07/98	09/30/98	Y	N	N
239453	CEB1/IO	09/30/97	12/02/97	Y	N	N
242618	RRB4/IO	01/29/98	02/10/98	Y	N	N
256522	CEB1/IO	06/02/99	06/07/99	Y	N	N
240966	RAB2/IO	11/20/97	12/12/97	Y	N	N
240967	RAB2/IO	11/20/97	12/12/97	Y	N	N
244091	TOX1/IO	03/11/98	03/12/98	Y	N	N
255365	CEB1/IO	04/20/99	04/30/99	Y	N	N
256746	ERB1/IO	06/10/99	07/19/99	Y	N	N
238908	IRB	09/10/97	12/09/97	Y	N	N

DP BARCODE: D244620 REREG CASE # 0248

CASE: 818961 DATA PACKAGE RECORD (CONTINUED) DATE: 12/03/99
SUBMISSION: S529758 BEAN SHEET

* * * ADDITIONAL DATA PACKAGES FOR THIS SUBMISSION * * *

DP BC	BRANCH/SECTION	DATE OUT	DUE BACK	INS	CSF	LABEL
244620	ERB1/IO	03/26/98	07/24/98	Y	N	N