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HUMAN HEALTH RISK ASSESSMENT

Fenthion

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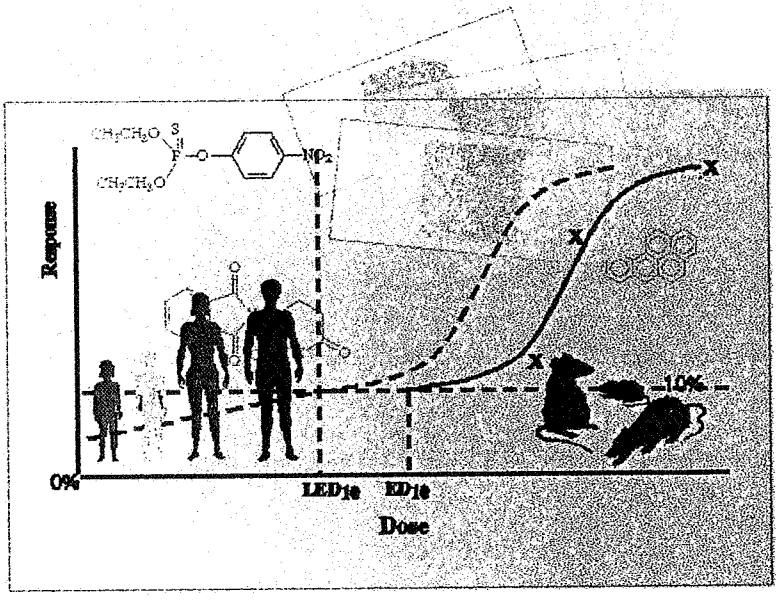

U.S. Environmental Protection Agency
Office of Pesticide Programs
Health Effects Division (7509C)

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October 13, 1999

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HUMAN HEALTH RISK ASSESSMENT

Fenthion

Phase 5

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Introduction

This revised human health risk assessment for fenthion incorporates the comments received from the U.S. Department of Agriculture, two new toxicity studies generated by Bayer Corp., and the most recent risk assessment techniques and policies. The hazard component of the risk has been reassessed to reflect recently-submitted oral acute and subchronic rat neurotoxicity studies, a recalculated dermal absorption factor, and the current Agency policy regarding use of human studies in risk assessment. Probabilistic reassessment of acute dietary risk has been conducted using the DEEM™ Software, revised usage (percent livestock treated) data, the hazard endpoint and dose derived from an animal study rather than a human study, and the reduced FQPA Safety Factor. Chronic dietary risks were revised using DEEM™, new usage data, the reduced FQPA factor, and the hazard component derived from an animal study. Occupational and residential risks were refined using several new exposure assumptions, revised dermal absorption factor, and hazard endpoints and doses derived from an animal study. A qualitative assessment of the potential exposure to fenthion through drinking water was conducted. Aggregate acute and chronic risks resulting from dietary exposure (food and drinking water) and residential exposure were assessed.

II. Executive Summary

The Health Effects Division (HED) of EPA's Office of Pesticide Programs has evaluated the fenthion database and conducted a revised human health risk assessment for fenthion. This assessment supersedes the 4/29/98 preliminary risk assessment (made publicly available) and the 2/18/99 assessment, which incorporated the public comments received on the 4/29/98 assessment. It also supersedes the 3/5/99 revised assessment concerning the foods contributing significantly to dietary risk.

Fenthion [*O,O*-dimethyl *O*-(4-(methylthio)-*m*-tolyl)phosphorothioate] is an organophosphate insecticide registered in the United States for use as a mosquito adulticide and larvicide, for direct livestock treatments, and in aquaculture as per Special Local Need registrations [24(c)]. Use as an adulticide is restricted to FL. Fenthion is rarely used as a mosquito larvicide; however, occupational risk assessments were conducted reflecting larvicidal use of three granular formulations likely to be voluntarily canceled. There are six cholinesterase-inhibiting residues of toxicological concern, all of which are included in the tolerance expression at 40 CFR 180.214; these are fenthion, fenthion sulfoxide, fenthion sulfone, fenthion O-analog, fenthion O-analog sulfoxide, and fenthion O-analog sulfone. Fenthion is generally applied as a 95% ready-to-use product (RTU) using ground fogging or aerial equipment for adult mosquito control in FL. For larvicidal use, granular products are applied. In the case of livestock, fenthion is applied to cattle and swine as impregnated ear tags or as a pour-on treatment. Fenthion is formulated as soluble concentrates, ready-to-use products, and impregnated material (ear tag). Exposures are expected through the diet, principally as residues in beef meat and fat. The Agency also expects exposure to occur to those involved in the application of fenthion. Residential exposure to fenthion is expected as a result of the mosquito adulticide use.

As with other organophosphates, the principal toxic effects induced by fenthion are related to its cholinesterase-inhibiting (ChE) activity. Fenthion is one of the more potent cholinesterase inhibitors, having an acute No Observed Adverse Effect Level (NOAEL) of 0.07 mg/kg/day in a 2-year oral monkey study; this study is useful for both acute dietary and short-term dermal/inhalation risk assessment because there was a lack of plasma and red blood cell (RBC) ChE inhibition at the NOAEL **during the first week of the study**. The short-term/acute Lowest Observed Adverse Effect Level (LOAEL) from the monkey study was 0.2 mg/kg/day based on observed plasma and RBC ChE inhibition. A 28-day human oral dosing study yielded similar results as marginal plasma ChE inhibition was observed at 0.07 mg/kg/day at 24 hours whereas neither RBC ChE inhibition nor clinical signs were observed. The dose to be used in the assessment of chronic dietary risk as well as intermediate-term dermal and inhalation risk is a threshold NOAEL/LOAEL of 0.02 mg/kg/day based on plasma ChE inhibition in the 2-year oral dosing monkey study. For occupational and residential risk

calculations, 3% dermal absorption [see 9/21/99 report of HED's Hazard Identification Assessment Review Committee (HIARC)] and 100% inhalation absorption were applied. Refer to Table 1 for fenthion acute toxicity and Table 2 for selction of endpoints and doses for use in risk assessment.

It is current Agency policy to make no final regulatory decision based on a human study until a new policy has been developed to ensure that such studies meet the highest scientific and ethical standards. In the absence of a policy, the Agency has selected doses and endpoints to calculate dietary and non-dietary risk based solely on animal studies.

The body of fenthion toxicology data includes a 28-day human study. In the preliminary fenthion human health risk assessment–released before the current Agency policy was articulated–this study provided the endpoint from which the Reference Doses (RfDs) and Population Adjusted Doses (PADs) were calculated. In the refined fenthion risk assessment presented here, this study and its role in the assessment have been reconsidered. Toxicity endpoints and doses have been selected, uncertainty factors have been assigned, and RfDs and PADs have been calculated based on the weight of the evidence, and the calculations begin from an animal NOAEL. In addition, the human study itself was reclassified as 'supplementary,' because it included only male subjects and was of limited power.

In this refined assessment the Agency calculates and presents the acute dietary and other short-term risk figures in two ways. The first calculation reflects no consideration at all of the human study, in any way or for any purpose. This is the calculation that the Agency is using for this risk assessment. The starting point for the RfD calculation is an animal NOAEL, and the full 10X interspecies uncertainty factor is applied. The second calculation, displayed here for illustrative purposes, also begins with an animal NOAEL, but the interspecies uncertainty factor is reduced from 10X to 3X, because of the similarities of response in the human study and the animal (monkey) study from which the endpoint was taken. If the eventual Agency policy permits consideration of this human study, this alternative could be appropriate.

In any event, the duration of the human study is too short for it to be considered in chronic dietary or intermediate-term risk assessments, and no comparable adjustment in the interspecies uncertainty factor is illustrated.

Upon applying the appropriate uncertainty factors, the derived Reference Doses (RfDs) used in risk assessment are 0.0007 mg/kg/day for acute dietary and 0.00007 mg/kg/day for chronic dietary assessments. The very low numerical values (high toxicity) of the hazard components of the risk are major contributors to the dietary risk. In the case of the dermal and inhalation routes of occupational and residential exposure, exposures were compared to target Margins of Exposure (MOEs) of 100 for short-term and 300 for intermediate-term durations of exposure. In the case of short-term risk assessments, exposures were also compared to a target MOE of 30 for illustrative purposes to reflect use of the human study to reduce the interspecies extrapolation uncertainty factor from 10X to 3X. Long-term exposure durations are not expected based on the current use pattern of fenthion products. There was no evidence of fenthion-induced carcinogenicity. There were no developmental toxicity, no increased sensitivity of offspring, and no neuropathological effects associated with fenthion.

The Food Quality Protection Act (FQPA) of 8/3/96 requires that a 10-fold safety factor be applied to risk assessments to protect against the potential increased sensitivity of infants and children and that this factor may be reduced by the Agency provided the available data indicate the lack of increased sensitivity. In the case of fenthion, hazard and exposure considerations led to the conclusion that this factor should be removed (reduced to 1X) rendering the acute and chronic RfDs equivalent to the respective Population Adjusted Doses (PADs) which are derived by dividing the RfD by the FQPA Safety Factor (see FQPA Safety Factor Committee report dated 8/6/98).

Dietary risk assessments reflected moderately refined exposure estimates; anticipated residues and percent-livestock-treated figures were incorporated. Refinements permit more realistic food exposure estimates such that the relative contribution of drinking water and residential exposure to the total aggregate exposure can be better evaluated. A probabilistic/Monte Carlo type of acute dietary risk assessment was conducted using an acute PAD (aPAD) of 0.0007 mg/kg/day; acute risks to the various population subgroups were **340-800% of the aPAD**, with the highest risk being to children (1-6 years). If the human study were used supportively to reduce the interspecies UF from 100X to 30X, acute dietary risks would still exceed the Agency's level of concern; risk estimates would be reduced roughly by a factor of three, i.e., to approximately 110-270% of the aPAD. Chronic risks were calculated using a chronic PAD (cPAD) of 0.00007 mg/kg/day; chronic dietary risks were 51-100% cPAD for the infant subgroups and females (13-50) and were **120-270% of the cPAD** for all other population subgroups, again, with the highest risk to children (1-6 years). Refer to Table 3 for details of the acute and chronic dietary exposures and risk calculations.

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The only potential dietary exposure via drinking water is surface water in Florida as a result of the mosquito adulticide use; even then, exposure is expected to be small because the application rate is low (0.05-0.1 lb ai/A) and because the key to controlling adult mosquitos is application such that minute fenthion droplets (generated via fogging or ultralow volume treatments) remain airborne for as long as possible to increase the opportunity for droplets to contact a mosquito. Fenthion, being a relatively nonvolatile liquid at environmental temperatures, is amenable to such applications. This application technique facilitates drift, reduces deposition, and widens the area of deposition. As a means of estimating the relative magnitude of potential risk associated with fenthion in drinking water compared to food and residential sources, EECs were compared to the PADs. Modeled fenthion exposure estimates due to drinking water alone (i.e., without considering food sources) indicate that roughly 5-20% of the aPAD and 10-30% of the cPAD could maximally be utilized by residues in drinking water alone. There is little concern for adults and children from exposure to fenthion in drinking water because: (i) the EECs utilized in these calculations were derived from conservative, screening-level models; (ii) only minor exposure to surface water is possible due to the application rate and method; and (iii) because the targeted treatment areas are residential which are not common contributors to drinking water derived from surface water sources.

Residential postapplication exposure scenarios were also considered. No chemical-specific or scenario-specific data are available for fenthion; therefore, the residential SOPs were used to estimate exposure. There are no risk concerns for exposure of adults associated with any treatment scenario as MOEs greatly exceeded each of the Agency's uncertainty factors, i.e., the target MOEs of 100 for short-term (30 using supportive human data) or 300 for intermediate-term. Likewise, MOEs for toddlers following ground-based fogging treatments, even when dermal and nondietary ingestion exposures were combined using likely conservative approaches, exceeded each of the Agency's uncertainty factors, i.e., short-term and intermediate-term risks to toddlers resulting from ground-based fogging were not of concern. Combined toddler MOEs resulting from aerial application did not exceed the uncertainty factor of 100 until 2 days after application at the average application rate and until 8 days after application at the maximum application rate (see Table 4); there is thus concern for short-term residential exposures to toddlers when the human study is not used supportively to reduce the interspecies uncertainty factor. However, if the human study were used to reduce the interspecies UF from 100X to 30X, short-term MOEs for toddlers would not be of concern when fenthion is applied aerially, even if dermal and nondietary ingestion exposures are combined on the day of application. Combined MOEs for toddlers are

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below the intermediate-term target MOE of 300 following aerial application (see average combined MOE in Table 4); therefore, intermediate-term risk to toddlers resulting from aerial treatments exceed the Agency's level of concern. The use of the results of the intermediate-term assessment should be interpreted with the understanding that no exposure or turf transferable residue (the measure of environmental concentration used for risk assessment purposes) dissipation data are available.

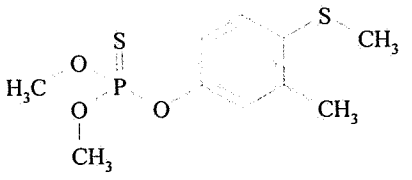
Aggregate exposure is comprised of food and water sources of dietary exposure as well as residential exposure to fenthion. Acute and chronic dietary (food only) assessments result in risks that exceed the Agency's level of concern. Similarly, combined residential dermal and nondietary ingestion exposures following aerial mosquito adulticide treatments result in risks of concern to toddlers. Sufficient data are not available to permit quantitative estimation of risks associated with fenthion in drinking water; however, significant contributions to the aggregate risk are not expected. Thus, the Agency is concerned about acute and chronic aggregate risks (dietary sources only) and short-term/intermediate-term aggregate risks.

The Agency has occupational handler risk concerns over the use of fenthion. The Agency evaluated exposures to occupational handlers in each of the three major markets for fenthion including mosquito control, livestock treatments, and applications in aquaculture (refer to Tables 5 and 6). For mosquito control adulticide applications, the Agency has concerns for loaders when using liquid formulations in preparation for mosquito adulticide applications of fenthion, in part, due to the very large acreages treated (lowest short-term MOE ~20). The Agency also has concerns for pilots and ground applicators during adulticide applications. For mosquito larvicide applications of granular products, the Agency has concerns for pilots during aerial application and for individuals completing ground applications. MOEs for loaders in these scenarios, however, exceeded the Agency's uncertainty factors, i.e., risks were not of concern. The Agency believes that the use of human flaggers is minimal during mosquito control applications but completed an assessment for these individuals. The MOEs associated with these job functions exceeded each of the Agency's uncertainty factors, indicating a lack of concern. Regarding occupational scenarios involving the treatment of livestock, the Agency has concerns for the ladle-on and ear tag placement exposures due to a lack of data with which to complete the assessment. MOEs for the ready-to-use livestock pour-on treatment package exceeded each of the Agency's uncertainty factors, i.e., such use does not pose a risk concern. The Agency has risk concerns for the use of fenthion in aquaculture, which involves the same individual loading and applying liquid formulations to ponds. No occupational postapplication exposure is expected based on the fenthion use pattern.

The fenthion database is not complete although it is sufficient for the conduct of this revised human health risk assessment. Confirmatory data remaining outstanding include: a general rat metabolism study, a dominant lethal assay, information to upgrade the ruminant and swine metabolism studies, recovery data for fenthion sulfoxide using FDA multiresidue methods, and cattle magnitude of the residue data reflecting direct animal treatment (ear tag and pour-on). No data are available that are directly applicable to the occupational and residential risk assessments. These assessments could be greatly refined with the generation of data. Any applicable chemical-specific or scenario-specific occupational and residential exposure data will be identified as the Agency participates in the risk mitigation process.

II. Physical and Chemical Properties

Fenthion [*O*,*O*-dimethyl *O*-(4-(methylthio)-*m*-tolyl)phosphorothioate] is an organophosphate insecticide registered in the U.S. as a mosquito adulticide and for direct livestock treatments.



A. Physical Properties

Physical state:	Liquid
Boiling point:	87 C at 0.01 mmHg
Solubility:	Soluble in alcohols, hexane, toluene, and chlorinated hydrocarbons; low water solubility (55 mg/L)
Vapor pressure:	3×10^{-5} mmHg at 20 C
Stability:	Stable up to 210 C; stable up to pH 9

B. Other Identifying Characteristics and Codes

Empirical Formula:	$C_{10}H_{15}O_3PS_2$
Molecular Weight:	278.3 g/mole
CAS Registry No.:	55-38-9
Shaughnessy No.:	053301

III. Hazard Assessment

The Toxicology Chapter of the RED was prepared by J. Doherty (1/26/96; D220510). Fenthion is a cholinesterase inhibitor that produces clinical signs including, but not limited to, muscle fasciculations, ataxia, tremors, decreased motor activity, repetitive chewing, gait impairment, decreased body temperature, and miosis in rats and rabbits.

Fenthion is classified as Toxicity Category II for acute oral, dermal, and inhalation toxicity (6/2/99 HIARC report). This chemical was classified Toxicity Category III for eye irritation and Category IV for dermal irritation. Acute toxicity studies did not reveal any gender bias in the toxicity profile of fenthion. Acute dermal and inhalation studies resulted in mortalities. In the acute dermal study for fenthion, the LD_{50} for both sexes combined was 963 mg/kg/day. In the case of the acute inhalation study the LC_{50} was 0.507 mg/L and 0.454 mg/L for males and females, respectively. Refer to Table 1 for acute toxicity of fenthion, used largely for labeling purposes. No dermal absorption study is available in the fenthion database. The dermal absorption factor for fenthion was calculated by HIARC to be approximately 3% based on comparison of the LOAEL from the oral developmental toxicity study in rabbits and the 21-day dermal toxicity study in rabbits (9/21/99 HIARC report).

A special 28-day cholinesterase inhibition study was conducted using male human subjects. While no clinical signs of toxicity were reported in this study, plasma cholinesterase inhibition was seen at 0.02 mg/kg/day one week after initiation of the dosing regimen. A marginal reduction in plasma cholinesterase activity was also seen at 0.07 mg/kg/day 24 hours after the first dosing period. As a result, 0.02 mg/kg/day was considered to be the NOAEL/LOAEL threshold dose. A similar threshold value was reported in the chronic oral toxicity study in monkeys.

Fenthion does not appear to elicit acute delayed neurotoxicity in hens. An Acute Neurotoxicity Study revealed a myriad of clinical signs that included muscle fasciculations, decreased body temperature, miosis, repetitive chewing, gait impairments, decreased body weight and decreased body weight gain. With the exception of decreased body weight and increased incidence of muscle fasciculations, no clinical signs of toxicity were reported in the Subchronic Neurotoxicity Study. This study was conducted with Wistar rats instead of Fisher 344 rats as requested by the Agency. It appears the Fisher rats provide a better estimate of this chemical's effects on the eye and optic nerve.

Developmental Toxicity Studies in the rat and rabbit do not demonstrate signs of developmental toxicity or enhanced sensitivity of the conceptus to fenthion. The Developmental Toxicity Study in the Rat showed no signs of developmental toxicity at the highest dose tested. In the rabbit, a **slight** increase in resorptions and unossified metacarpals were the only signs of developmental toxicity observed during the Developmental Toxicity Study. Interestingly, the Multi-Generational Reproduction Study showed signs of parental toxicity, and reproductive toxicity (decreases in number of implantation sites, fertility index, number of viable litters, and number of total pups) as well as signs of decreased pup viability and decreased pup growth.

The Agency has requested that a new Dominant Lethal Mutagenicity Study be submitted for review. This request is based on the fact that fenthion was demonstrated to be a potential mutagen in two mutagenicity studies (Unscheduled DNA Synthesis and Mouse Micronucleus Assay). Fenthion **did not** show evidence of mutagenicity in the Bacterial Reverse Mutation Test or in the *In Vitro* Chromosome Aberration Test in Chinese Hamster Ovary Cells.

Fenthion is not considered a carcinogen and is, therefore, classified as a Group E chemical, suggesting that it is "Not Likely" to be carcinogenic in humans via relevant routes of exposure. This classification is based on acceptable studies in two animal species (mouse and rat).

Chronic Toxicity Studies are available in the rat, dog, and monkey. The dog and monkey Chronic Toxicity Studies did not reveal any systemic signs of toxicity due to prolonged exposure to fenthion with the exception of cholinesterase inhibition. In the rat study, however, epididymal pathology, vacuolation of the nasolacrimal duct, and ocular pathology were some of the signs of toxicity reported after long-term exposure to this chemical.

IV. Dose Response and Hazard Endpoint Slection

A. Endpoints

Conventionally, when a NOAEL from an animal study is selected, an uncertainty factor of 100 (10x for interspecies extrapolation and 10x for intraspecies variation) is used. This was the case for chronic dietary and intermediate-term occupational/residential risk assessments. However, the HIARC (6/2/99 report) determined that an uncertainty factor of 30 (10x for intraspecies variation and 3x for interspecies extrapolation) would be adequate for the acute dietary risk assessment as well as short-term occupational and residential risk assessments. The HIARC concluded that the interspecies factor could be reduced since a supplemental 28-day human oral dosing study is supportive of the NOAEL derived from the monkey study due to marginal (about 8%) plasma ChE inhibition observed in humans at 24 hours with neither clinical signs nor RBC ChE inhibition observed. The HIARC determined that a 3x interspecies extrapolation factor is necessary because, although it was not rigorous enough for endpoint selection due to limited test power and lack of female test subjects, the human study was supportive of the monkey study. However, it is current Agency policy that a regulatory decision cannot be made using a human study until a decision on the ethics of such use has been made. As of this date, such a decision has not been made. Consequently, the official position is to assess the full 10X to compensate for interspecies extrapolation; the acute and short-term risk assessments thus incorporate the full 10X factor. For comparative purposes, however, the affected risk assessments will also be presented utilizing reduction of the interspecies factor to 3X.

A summary of the fenthion toxicology studies and hazard dose and endpoint selections made by the HIARC is provided in the 6/2/99 HIARC report. Table 1 contains the acute toxicity endpoints which are especially important for labeling purposes, eg. for label warnings and the level of personal protective equipment (PPE) necessary for fenthion handlers. Table 2 contains a summary of the hazard doses and endpoints selected for use in the various human health risk assessments.

Table 1. Fenthion Acute Toxicity

Study	Results	Toxicity Category
81-1. Acute Oral-rats. MRID No.: 40186704.	LD_{50} = 405 (302-681) mg/kg, males = 586 (461-791) mg/kg females	II
81-2. Acute Dermal -rabbits. MRID No.:40186705.	LD_{50} = 963 (744-1162) mg/kg for both sexes combined	II
81-3. Acute Inhalation - rats. MRID No.: 40186706	LC_{50} = 0.507 (0.409 - 0.695) mg/L, males = 0.454 (0.349- 0.658) mg/L, females Deaths in females and tremors and ataxia (both sexes) at lowest doses (0.209 mg/L).	II
81-4. Primary Ocular Irritation - rabbits. MRID No.: 40186708	No cornea or iris irritation was noted. Discharge, redness and swelling were noted in the conjunctiva in all rabbits that were reversed after two days.	III
81-5. Primary Dermal Irritation - rabbits. MRID No.: 40186709	PII = 0	IV
81-6. Dermal Sensitization - guinea pigs. MRID No.: 40186710	Not a sensitizer in the Magnusson-Kligman maximization study	NA--
81-7. Delayed type neurotoxicity-hens. MRID No.: 40229201	No evidence of delayed type neurotoxicity following oral (40 mg/kg > acute LD_{50} or dermal (200 mg/kg).	NA--
81-8. Acute Neurotoxicity - rats MRID No.: 44326401	NOAEL for cholinesterase inhibition <1 mg/kg/day (LDT) in both sexes.	NA--

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Table 2. Fenthion Hazard Dose and Endpoint Selection for Risk Assessment

EXPOSURE PERIOD	DOSE/UF	ENDPOINT	STUDY	MOE
Acute Dietary	NOAEL = 0.07 mg/kg	Lack of plasma cholinesterase inhibition at week 1 measurement	Chronic-Monkey	Not Relevant
	UF = 100[b]	**Acute RfD = 0.0007 mg/kg**		
Chronic Dietary	NOAEL/LOAEL = 0.02 mg/kg/day (threshold dose)	Plasma cholinesterase inhibition	Chronic-Monkey	Not Relevant
	UF = 300[c]	**Chronic RfD = 0.00007 mg/kg/day**		
Dermal Absorption	3% estimated based on the oral LOAEL of 2.75 mg/kg/day in the oral developmental toxicity study and the dermal LOAEL of 100 mg/kg/day in the 21-day dermal toxicity study in rabbits based on a common endpoint (cholinesterase inhibition)			
Short-Term (Dermal & Inhalation)[a]	Oral NOAEL = 0.07 mg/kg/day	Lack of plasma cholinesterase inhibition at week 1 measurement	Chronic-Monkey	100 [b]
Intermediate-Term (Dermal & Inhalation)[a]	Threshold NOAEL/LOAEL 0.02 mg/kg/day	Plasma cholinesterase inhibition	Chronic-Monkey	300 [c]
Long-Term (Dermal & Inhalation)[a]	Threshold NOAEL/LOAEL 0.02 mg/kg/day	Plasma cholinesterase inhibition	Chronic-Monkey	300 [c]

[a]Oral values were selected; therefore route-to-route extrapolation must be used (3% dermal absorption)

[b]UF (for acute dietary) or MOE (for short-term assessments) would be 30 if the human study were considered jointly with the monkey study.

[c]UF (for chronic dietary) or MOE of 300 (for intermediate- or long-term assessments) is due to the lack of a definite NOAEL in the critical study.

Note: MOEs are for occupational and residential exposure risk assessments.

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B. FQPA Safety Factor

The FQPA Safety Factor Committee evaluated the hazard and exposure data for fenthion as bases for making a recommendation on the magnitude of the FQPA Safety Factor (as required by FQPA). The FQPA Safety Factor Committee recommendation in the 8/6/98 report was that the FQPA safety factor be **removed (reduced to 1X)** for fenthion. The rationale for removal (reduction to 1X) of the FQPA Safety Factor is:

(i) The data provided no indication of increased susceptibility of rats or rabbits to *in utero* and/or postnatal exposure to fenthion.
(ii) No evidence of developmental anomalies, including abnormalities in the development of fetal nervous system was observed in the pre- and/or postnatal studies.
(iii) There are no data gaps for the critical studies used to determine increased sensitivity of infants and children.

For dietary risk assessments, the target exposure level above which risk is considered to be of concern is referred to as the Population Adjusted Dose (PAD). An acute PAD (aPAD) and a chronic PAD (cPAD) are calculated by dividing the respective acute and chronic RfDs (aRfD and cRfD) by the FQPA Safety Factor. As the FQPA Safety Factor was reduced to 1X in the case of fenthion, the aPAD and cPAD are identical to the respective aRfD and cRfD (Table 2).

V. Dietary Exposure and Risk Assessment

A. Food Sources of Dietary Exposure

Existing and reassessed tolerances are established for the combined residues of fenthion and its cholinesterase-inhibiting metabolites in or on livestock commodities (40 CFR §180.214). The phosphorylated (cholinesterase-inhibiting) metabolites include fenthion oxygen analog (oxon); fenthion sulfoxide; fenthion sulfone; fenthion oxygen analog sulfoxide; and fenthion oxygen analog sulfone. Adequate data collection and enforcement methods are available to detect fenthion residues in livestock commodities. No tolerances have been established for fenthion residues in/on plant commodities.

Fenthion uses that can result in dietary exposure are limited to ear tag use, pour-on applications, and the veterinary feed-through uses for cattle and swine. Anticipated upper bound residue levels in livestock commodities were calculated using the limited available data. Upper bound estimates of fenthion residues in milk, beef, and pork commodities were described in detail in the C. Olinger memo dated 9/30/97 (DP Barcode D238981). No new data have been submitted. To further refine the exposure and risk estimates for fenthion, BEAD/OPP provided HED with upper bound estimates of the percentage of cattle and swine treated with fenthion (A. Halvorson memorandum dated 2/4/99). The BEAD estimates for dairy cattle, beef cattle, and swine are 4%, 12%, and 9% of animals treated, respectively.

Anticipated residues (ARs) were determined based on a 21-day preslaughter interval (PSI), which HED agreed could remain on existing labels in order to harmonize with the veterinary feed-through use established under the purview of the FDA [HED generally allows for a maximum PSI of 3 days]. Fenthion residues in milk were monitored by USDA/PDP in 1996 and 1997; a total of 1,297 samples were analyzed with no detections. The limit of detection (LOD) for fenthion was 0.001 ppm for all USDA/PDP laboratories. The milk monitoring data and the 21-day PSI residue estimates were used in the acute and chronic analyses. These anticipated residue levels in livestock commodities were corrected by the percentage of livestock treated figures provided by BEAD.

HED conducts dietary risk assessments using the Dietary Exposure Evaluation Model (DEEM™), which incorporates consumption data generated in USDA's Continuing Surveys of Food Intakes by Individuals (CSFII), 1989-1992. For chronic dietary risk assessments, the three-day average of consumption for each subpopulation is combined with residues in commodities to determine average exposure in mg/kg/day. For refined acute dietary risk assessments, the entire distribution of consumption events for individuals is multiplied by a distribution of residues (probabilistic analysis, referred to as "Monte Carlo;" risk at 99.9th percentile of exposure reported) to obtain a distribution of exposures in mg/kg/day.

The acute and chronic dietary exposure and risk estimates exceed the Agency's level of concern for the general U.S. population and various population subgroups, including infants and children (C. Swartz, 10/12/99, D259939). The most highly exposed subgroup is children 1-6 years, with approximately 800% aPAD (at the 99.9th percentile of exposure) and 270% cPAD consumed. In the chronic analysis, infants were the only population subgroup for which chronic dietary risk was below the level of concern, at approximately 60% cPAD. Detailed results are shown in Table 3. The acute critical exposure contribution and the chronic critical commodity analyses demonstrate that estimated dietary risk is due largely to potential residues in beef meat and fat and that milk is a minor contributor to acute and chronic dietary risk.

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Available USDA monitoring data on beef liver did not include all fenthion residues of concern, but qualitatively support the results of the dietary exposure analyses conducted using livestock direct treatment study data.

The chronic and acute analyses do not take into consideration the potential for reduction of fenthion residues in cooked/canned/processed livestock commodities, since there are no chemical-specific cooking studies. HED will refine the fenthion dietary exposure analyses if such data become available.

Table 3. Acute and Chronic Dietary Exposure/Risk Estimates for Fenthion

Population Subgroup	Acute Assessment (99.9th %-ile)		Chronic Assessment	
	Exposure (mg/kg/day)	%aPAD	Exposure (mg/kg/day)	%cPAD
General US Population	0.003274	470	0.000094	130
All Infants (<1 yr)	0.004124	590	0.000040	57
Nursing Infants (<1 year old)	0.003312	470	0.000036	51
Non-Nursing Infants (<1 yr)	0.004350	620	0.000042	60
Children (1-6)	0.005627	800	0.000187	270
Children (7-12 years)	0.003709	530	0.000135	190
Females (13-19 years)	0.002893	410	0.000087	120
Females (13-50 years)	0.002390	340	0.000073	100
Males (13-19 years)	0.002772	400	0.000116	170
Males (20+ years)	0.002509	360	0.000088	130

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B. Drinking Water Sources of Dietary Exposure

A drinking water health advisory level for fenthion and/or fenthion metabolites has not been established. Limited groundwater monitoring data are available but the utility of these data are limited by the fact that only the parent compound was analyzed; fenthion per se is not as persistent as the five regulated metabolites of toxicological concern. In addition, Florida was not tested (Florida is the principal state in which fenthion is used as a mosquito adulticide). There are no terrestrial agricultural uses of fenthion; these uses represent the primary drinking water source of exposure. Therefore, the potential for drinking water exposure is very low. The Agency believes that the only use that could potentially cause contamination of drinking water is the mosquito use which involves aerial applications and/or ground applications in thirteen counties in Florida.

Fenthion mosquito uses are largely adulticide applications that are limited to residential spraying for mosquito control.

Fenthion is either contained within an ear tag or is spot treated to livestock; these uses are not expected to result in significant exposures to drinking water sources. Fenthion is used in mosquito treatment largely as an adulticide, which requires the active ingredient to remain suspended in air for a period of time, rather than quickly settling out. Fenthion, being a relatively nonvolatile liquid at environmental temperatures, is amenable to such applications. This application technique, in effect, facilitates drift, reduces deposition, and widens the area of deposition. There is potential for this use to result in **surface water** exposure from spray drift.

A conservative screening level estimate of potential fenthion residues in surface water was generated using the GENEEC model. These Estimated Environmental Concentrations (EECs) were developed for a 1 ha by 2 m deep pond adjacent to a 10 ha treated area. Inputs to GENEEC included an assumption of 12 applications at 7 day intervals at a rate of 0.1 lb ai/acre, an assumed aerial spray drift of 5%, an assumed soil half-life of 3 days, a K_{oc} value of 1500, and an assumed aquatic half-life of 6 days. Over a 3-year period from 1993-1996, fenthion was applied in Lee County, FL an average of approximately 4 times/month.

The EECs thus generated are to be used for determining potential drinking water exposure and risk. The peak concentration for determination of acute exposure and risk is 1.33 μg/L and the 56-day average concentration for determination of chronic exposure and risk is 0.19 μg/L.

As a means of estimating the relative magnitude of potential risk associated with fenthion in drinking water compared to food and residential sources, these EECs were compared to the PADs. Conservatively modeled fenthion exposure estimates due to drinking water alone (i.e., without considering food sources) indicate that roughly 5-20% of the aPAD and 10-30% of the cPAD could maximally be utilized by residues in drinking water alone. There is little concern for adults and children from exposure to fenthion in drinking water because: (i) the EECs utilized in these calculations were derived from conservative, screening-level models; (ii) only minor exposure to surface water is possible due to the application rate and method; and (iii) because the targeted treatment areas are residential which are not typically contributors to drinking water derived from surface water sources.

VI. Occupational and Residential Exposure and Risk Assessment

A. Use Pattern, Assumptions, and Other Information

Mosquito control chemicals can be used as larvicides or adulticides. Larvicide applications are typically added directly to stagnant and other waters where breeding occurs. Adulticide applications are made in a manner that suspends as many small droplets in the air as possible since the efficacy of the chemical is dependent upon contacting the mosquitoes in flight. The principal use of fenthion for mosquito control is as an adulticide. Fenthion can be applied using a wide array of application equipment. Mosquito adulticide applications are made using either thermal or nonthermal fogging equipment. Most of these applications are completed with nonthermal fogging equipment on the ground or through aerial application. In agriculture, animals are treated by ear tag, pour-on, or ladle-on methods. Aquaculture applications are completed using handheld equipment such as low pressure handwand sprayers and backpack sprayers. Mosquito control applications are completed at the discretion of mosquito control districts. Animal treatments are completed usually as needed and aquaculture applications are completed prior to stocking fishponds.

Because of the way that fenthion is applied, the Agency considered exposures to those who occupationally apply fenthion (i.e., referred to as handlers) and also to the general population in areas that have been subjected to mosquito control applications (i.e., referred to as residential postapplication exposure). The Agency does not believe that there are individuals who are exposed after applications during the course of employment (i.e., referred to as occupational postapplication). Fenthion is also not available for sale to the general public. Therefore, the Agency also did not consider the exposure of people in the general public that would purchase and use it (i.e., referred to as homeowner handlers).

No chemical-specific handler exposure data were submitted in support of the reregistration of fenthion. As a result, the Pesticide Handlers Exposure Database (PHED) was used to complete all occupational handler risk assessments. Available use and usage information were also included as appropriate (e.g., average application rates). The Agency evaluated postapplication residential risks by first calculating the amount of fenthion that deposits in areas after mosquito control applications and then calculating the exposures of both adults and children (i.e., toddlers are the sentinel population) in those environments. The Agency used the Spray Drift Task Force model for predicting deposition from aerial applications (i.e., AgDRIFT) to determine how much material deposits in residential areas after aerial applications and published data to determine how much material deposits in residential areas after ground-fogger applications. After these values were determined, the risks for adults and toddlers were calculated using guidance included in the Agency's *Standard Operating Procedures For Residential Exposure Assessment* and guidance provided at the recent meeting of the FIFRA Science Advisory Panel on residential exposure issues.

The risk assessment has been revised to incorporate recent changes in the hazard parameters including a revision of the dermal absorption factor from 20 to 3 percent and to address concerns over the use of a human toxicity study versus use of an oral administration study conducted in primates (monkeys). The Agency considers the duration of exposure in its risk assessments. In this case, short-term ($\leq$7 days) and intermediate-term exposures (>7 days) were considered as the Agency believes that fenthion exposures can occur in these patterns. Longer term (or chronic) exposures are not expected to occur based on the fenthion use pattern. Toxicological endpoints are unchanged from the previous risk assessment. For short-term exposures, the Agency selected an endpoint of 0.07 mg/kg/day while an endpoint of 0.02 mg/kg/day was selected for intermediate-term risk assessment (the effect for both durations of exposure is the inhibition of plasma cholinesterase inhibition). Both of these endpoints were selected from the monkey study and are also closely reflected in the human data. These endpoints were used to assess risks from all routes of exposure by route-to-route extrapolation. Note that dermal and inhalation risks were combined because the same oral-dosing study (monkey) served as the source of doses and endpoint for risk assessment and because the toxic effect (cholinesterase inhibition) was the same regardless of the duration of exposure in the monkey study. The Agency defines risk concerns by comparing expressions of risk, otherwise referred to as *Margins of Exposure (MOEs),* to uncertainty factors established by defining how closely the animal model upon which the endpoint is based relates to humans and the uncertainties associated with the selected endpoints.

The Agency is currently grappling with the ethical issues associated with the use of human toxicity testing. For fenthion, the uncertainty factors for short-term assessments (30 or 100) have been defined based on whether human data is used to characterize the results of the monkey study (i.e., uncertainty factor of 30) or if just the monkey study is used for defining the uncertainty factor (i.e., uncertainty factor of 100). The available human toxicity study is not applicable to intermediate-term duration exposures; however, there is not a definitive NOAEL at this duration so the uncertainty factor for all of these assessments is 300.

B. Residential Exposure and Risk

Residential postapplication exposure scenarios were also considered. There are no risk concerns for exposure of adults associated with any treatment scenario as MOEs greatly exceeded (MOEs >870) each of the Agency's uncertainty factors, i.e., the target MOEs of 100 for short-term (30 using supportive human data) or 300 for intermediate-term. Likewise, MOEs for toddlers following ground-based fogging treatments, even when dermal and nondietary ingestion exposures were combined, exceeded each of the Agency's uncertainty factors, i.e., short-term and intermediate-term risks to toddlers resulting from ground-based fogging were not of concern (MOE was 360 on the day of treatment at the maximum rate). Combined toddler MOEs resulting from aerial application did not exceed the uncertainty factor of 100 until 2 days after application at the average application rate and until 8 days after application at the maximum application rate (see Table 4); there is thus concern for short-term residential exposures to toddlers when the human study is not used supportively to reduce the interspecies uncertainty factor (UF). However, if the human study were used to reduce the interspecies UF from 100X to 30X, short-term MOEs for toddlers would not be of concern when fenthion is applied aerially, even if dermal and nondietary ingestion exposures are combined on the day of application. Combined MOEs for toddlers are below the intermediate-term target MOE of 300 following aerial application (see average combined MOE in Table 4); therefore, intermediate-term risk to toddlers resulting from aerial treatments exceeds the Agency's level of concern (Table 4). The use of the results of the intermediate-term assessment should be interpreted with the understanding that no exposure or turf transferable residue (the measure of environmental concentration used for risk assessment purposes) dissipation data are available.

Table 4. Combined Moes Attributable to Toddler Exposures in Areas Previously Treated with Fenthion Using Aerial ULV Equipment

DAT	Toddler Dermal Exposure MOEs		Toddler Hand-to-mouth MOEs		Toddler Object-to-mouth MOEs		Toddler Soil Ingestion MOEs		Toddler Combined MOEs	
	Average Appl. Rate	Maximum Appl. Rate	Average Appl. Rate	Maximum Appl. Rate	Average Appl. Rate	Maximum Appl. Rate	Average Appl. Rate	Maximum Appl. Rate	Average Appl. Rate	Maximum Appl. Rate
0	1670	935	91	51	2907	1628	216908	121469	83.6	46.8
1	1855	1039	101	57	3230	1809	241009	134965	92.9	52.0
2	2061	1154	112	63	3588	2009	267788	149961	103.3	57.8
3	2290	1283	125	70	3987	2233	297542	166624	114.7	64.2
4	2545	1425	138	78	4430	2481	330603	185137	127.5	71.4
5	2827	1583	154	86	4922	2756	367336	205708	141.6	79.3
6	3142	1759	171	96	5469	3063	408151	228565	157.4	88.1
7	3491	1955	190	106	6077	3403	453502	253961	174.9	97.9
8	3879	2172	211	118	6752	3781	503891	282179	194.3	108.8
9	4310	2413	234	131	7502	4201	559878	313532	215.9	120.9
10	4788	2681	260	146	8336	4668	622087	348369	239.9	134.3
AVG.	1537	861	84	47	2677	1499	199739	111854	77.0	43.1

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C. Occupational Exposure and Risk

Occupational and residential exposure and risk were revised by J. Dawson (10/1/99, D259765). Fenthion is a restricted-use organophosphate insecticide that is marketed in a variety of end-use products including liquid concentrates, ready-to-use solutions, impregnated articles (i.e., cattle ear tags); and granulars. Fenthion is primarily used as a mosquito control chemical, in agriculture on livestock to control flies and cattle lice, and in aquaculture to control dragonfly nymphs in ornamental fish ponds.

The Agency has risk concerns over the use of fenthion, particularly for occupational handlers (Tables 5 and 6). The Agency evaluated exposures to occupational handlers in each of the three major markets for fenthion including mosquito control, livestock treatments, and applications in aquaculture. For mosquito control adulticide applications, the Agency has concerns for loaders when using liquid formulations in preparation for mosquito adulticide applications of fenthion, in part due to the very large acreages treated (lowest short-term MOE ~20). The Agency also has concerns for pilots and ground applicators during adulticide applications. For mosquito larvicide applications, the Agency has concerns for pilots during aerial application and for individuals completing ground applications. MOEs for loaders in these scenarios, however, exceeded the Agency's uncertainty factors. The Agency believes that the use of human flaggers is rare during mosquito control applications but completed an assessment for these individuals to account for other people that may be exposed in a similar manner (e.g., ground observers). The risks associated with these jobs exceeded each of the Agency's uncertainty factors (i.e., MOE of 100 for short-term and 300 for intermediate-term) during granular applications but not for liquid applications (i.e., the Agency has risk concerns for liquid applications). For the treatment of food animals, the Agency has concerns for the ladle-on and ear tag placement exposures due to a lack of data with which to complete the assessment. MOEs for the ready-to-use pour-on package exceeded each of the Agency's uncertainty factors, i.e., there is no risk of concern. Additionally, the Agency has risk concerns for the use of fenthion in aquaculture. Details of the occupational risk calculations are presented in Tables 5 and 6.

TABLE 5. Fenthion MOEs Attributable to Combined Short-Term Dermal and Inhalation Exposures

Scen.	Scen. Descriptor	Crop Type Or Target	Exposure Factors		Summary Moes for Combinations of Dermal and Inhalation Protective Measures							
			Rate	Acres or Gallons	Baseline (Table 2)	Single Layer, Gloves & No Respirator (Tables 2 &3)	Single Layer, Gloves & Pf 5 Respirator (Table 3)	Single Layer, Gloves & Pf 10 Respirator (Tables 3 & 4)	Double Layer, Gloves & No Respirator (Tables 2 & 4)	Double Layer, Gloves & Pf 5 Respirator (Tables 3 & 4)	Double Layer, Gloves & Pf 10 Respirator (Table 4)	Eng. Controls (Table 5)
Occupational Mixer/loaders												
1a	Mixing/loading Liquids for Aerial Application	Mosquito Adulticide	0.1	7500	0.1	3.5	7.0	8.1	3.8	8.7	10.4	19.2
		Mosquito Adulticide	0.056	7500	0.1	6.2	12.5	14.4	6.8	15.6	18.5	34.2
1b	Mixing/loading Liquids for Ground Fogger Application	Mosquito Adulticide	0.03	3000	0.6	28.8	58.5	67.2	31.8	72.6	86.4	159.7
		Mosquito Adulticide	0.016	3000	1.2	54.0	109.8	126.0	59.7	136.1	162.0	299.4
2	Loading Granulars for Aerial Application	Mosquito Larvicide	0.1	800	31.4	32.1	112.0	162.5	34.0	138.6	225.2	1568.9
		Mosquito Larvicide	0.056	800	56.0	57.4	200.0	290.1	60.7	247.5	402.1	2801.6
		Mosquito Larvicide	0.1	80	313.8	321.2	1119.7	1624.7	339.9	1385.7	2251.8	15689.0
		Mosquito Larvicide	0.056	80	560.3	573.5	1999.5	2901.2	607.0	2474.5	4021.1	28016.1
OCCUPATIONAL APPLICATORS												
3	Aerial Application of Liquid Sprays	Mosquito Adulticide	0.1	7500	Not Feasible	Not Feasible	Not Feasible	Not Feasible	Not Feasible	Not Feasible	Not Feasible	30.0
		Mosquito Adulticide	0.056	7500	Not Feasible	Not Feasible	Not Feasible	Not Feasible	Not Feasible	Not Feasible	Not Feasible	53.5
4	Ground Fogger Application	Mosquito Adulticide	0.03	3000	3.6	4.7	6.7	7.1	4.9	7.3	7.7	53.4
		Mosquito Adulticide	0.016	3000	6.7	8.7	12.6	13.3	9.2	13.6	14.5	100.1
5	Aerial Application of Granulars	Mosquito Larvicide	0.1	800	Not Feasible	Not Feasible	Not Feasible	Not Feasible	Not Feasible	Not Feasible	Not Feasible	45.3
		Mosquito Larvicide	0.056	800	Not Feasible	Not Feasible	Not Feasible	Not Feasible	Not Feasible	Not Feasible	Not Feasible	81.0
		Mosquito Larvicide	0.1	80	Not Feasible	Not Feasible	Not Feasible	Not Feasible	Not Feasible	Not Feasible	Not Feasible	453.4

Scen.	Scen. Descriptor	Crop Type Or Target	Exposure Factors		Summary Moes for Combinations of Dermal and Inhalation Protective Measures							
			Rate	Acres or Gallons	Baseline (Table 2)	Single Layer, Gloves & No Respirator (Tables 2 &3)	Single Layer, Gloves & Pf 5 Respirator (Table 3)	Single Layer, Gloves & Pf 10 Respirator (Tables 3 & 4)	Double Layer, Gloves & No Respirator (Tables 2 & 4)	Double Layer, Gloves & Pf 5 Respirator (Tables 3 & 4)	Double Layer, Gloves & Pf 10 Respirator (Table 4)	Eng. Controls (Table 5)
		Mosquito Larvicide	0.056	80	Not Feasible	Not Feasible	Not Feasible	Not Feasible	Not Feasible	Not Feasible	Not Feasible	809.6
6	Ready-to-Use Package For Livestock	Fly Control	0.008	200	33.1	1543.2	3136.2	3600.8	1705.7	3888.9	4629.6	Not Feasible
7	Ear Tags For Cattle	Fly Control	0.013	200	No Data	No Data	No Data	No Data	No Data	No Data	No Data	Not Feasible
Occupational Mixer/loader/applicators												
8	Ladel On For Livestock	Fly Control	0.004	200	No Data	No Data	No Data	No Data	No Data	No Data	No Data	Not Feasible
9	Ground-based Granular Application	Mosquito Larvicide	0.1	5	27.1	28.7	33.6	34.4	42.0	53.3	55.2	Not Feasible
10	Low Pressure Handwand Application of 95% Liquid	Dragonfly Larvicide	0.8	5	0.4	28.6	64.8	77.0	29.8	71.6	86.9	Not Feasible
		Dragonfly Larvicide	0.8	2.5	0.8	57.1	129.6	154.1	59.6	143.3	173.8	Not Feasible
11	Backpack Application of 95% Liquid	Dragonfly Larvicide	0.8	5	No Data	11.7	15.1	15.7	15.7	22.7	24.0	Not Feasible
		Dragonfly Larvicide	0.8	2.5	No Data	23.3	30.2	31.4	31.4	45.4	48.0	Not Feasible
Flaggers												
12	Flagging For Aerial Application of Liquid Sprays	Mosquito Adulticide	0.1	7500	9.6	9.2	15.2	16.5	9.6	16.3	17.9	480.4
		Mosquito Adulticide	0.056	7500	17.2	16.4	27.1	29.5	17.2	29.2	32.0	857.8
13	Flagging For Aerial Application of Granulars	Mosquito Larvicide	0.1	800	261.8	309.3	785.3	972.2	340.3	1020.8	1361.1	13087.6
		Mosquito Larvicide	0.056	800	467.4	552.4	1402.2	1736.1	607.6	1822.9	2430.6	23370.7

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Table 6. Fenthion MOEs Attributable to Combined Intermediate-Term Dermal and Inhalation Exposures

Scen.	Scenario Descriptor	Crop Type Or Target	Exposure Factors		Summary Moes for Combinations of Dermal and Inhalation Protective Measures							
			Rate	Acres or Gallons	Baseline (Table 2)	Single Layer, Gloves & No Respirator (Tables 2 &3)	Single Layer, Gloves & PF 5 Respirator (Table 3)	Single Layer, Gloves & PF 10 Respirator (Tables 3 & 4)	Double Layer, Gloves & No Respirator (Tables 2 & 4)	Double Layer, Gloves & PF 5 Respirator (Tables 3 & 4)	Double Layer, Gloves & PF 10 Respirator (Table 4)	Eng. Controls (Table 5)
Occupational Mixer/loaders												
1a	Mixing/loading Liquids for Aerial Application	Mosquito Adulticide	0.1	7500	0.02	1.0	2.0	2.3	1.1	2.5	3.0	5.5
		Mosquito Adulticide	0.056	7500	0.04	1.8	3.6	4.1	1.9	4.4	5.3	9.8
1b	Mixing/loading Liquids for Ground Fogger Application	Mosquito Adulticide	0.03	3000	0.18	8.2	16.7	19.2	9.1	20.7	24.7	45.6
		Mosquito Adulticide	0.016	3000	0.33	15.4	31.4	36.0	17.1	38.9	46.3	85.5
2	Loading Granulars for Aerial Application	Mosquito Larvicide	0.1	800	8.97	9.2	32.0	46.4	9.7	39.6	64.3	448.3
		Mosquito Larvicide	0.056	800	16.01	16.4	57.1	82.9	17.3	70.7	114.9	800.5
		Mosquito Larvicide	0.1	80	89.65	91.8	319.9	464.2	97.1	395.9	643.4	4482.6
		Mosquito Larvicide	0.056	80	160.09	163.9	571.3	828.9	173.4	707.0	1148.9	8004.6
Occupational Applicators												
3	Aerial Application of Liquid Sprays	Mosquito Adulticide	0.1	7500	Not Feasible	Not Feasible	Not Feasible	Not Feasible	Not Feasible	Not Feasible	Not Feasible	8.6
		Mosquito Adulticide	0.056	7500	Not Feasible	Not Feasible	Not Feasible	Not Feasible	Not Feasible	Not Feasible	Not Feasible	15.3
4	Ground Fogger Application	Mosquito Adulticide	0.03	3000	1.02	1.3	1.9	2.0	1.4	2.1	2.2	15.3
		Mosquito Adulticide	0.016	3000	1.91	2.5	3.6	3.8	2.6	3.9	4.1	28.6
5	Aerial Application of Granulars	Mosquito Larvicide	0.1	800	Not Feasible	Not Feasible	Not Feasible	Not Feasible	Not Feasible	Not Feasible	Not Feasible	13.0
		Mosquito Larvicide	0.056	800	Not Feasible	Not Feasible	Not Feasible	Not Feasible	Not Feasible	Not Feasible	Not Feasible	23.1
		Mosquito Larvicide	0.1	80	Not Feasible	Not Feasible	Not Feasible	Not Feasible	Not Feasible	Not Feasible	Not Feasible	129.5

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Scen.	Scenario Descriptor	Crop Type Or Target	Exposure Factors		Summary Moes for Combinations of Dermal and Inhalation Protective Measures							
			Rate	Acres or Gallons	Baseline (Table 2)	Single Layer, Gloves & No Respirator (Tables 2 &3)	Single Layer, Gloves & PF 5 Respirator (Table 3)	Single Layer, Gloves & PF 10 Respirator (Tables 3 & 4)	Double Layer, Gloves & No Respirator (Tables 2 & 4)	Double Layer, Gloves & PF 5 Respirator (Tables 3 & 4)	Double Layer, Gloves & PF 10 Respirator (Table 4)	Eng. Controls (Table 5)
		Mosquito Larvicide	0.056	80	Not Feasible	Not Feasible	Not Feasible	Not Feasible	Not Feasible	Not Feasible	Not Feasible	231.3
6	Ready-to-Use Package For Livestock	Fly Control	0.0084	200	9.45	440.9	896.1	1028.8	487.3	1111.1	1322.8	Not Feasible
7	Ear Tags For Cattle	Fly Control	0.013	200	No Data	No Data	No Data	No Data	No Data	No Data	No Data	Not Feasible
Occupational Mixer/loader/Applicators												
8	Ladel On For Livestock	Fly Control	0.004	200	No Data	No Data	No Data	No Data	No Data	No Data	No Data	Not Feasible
9	Ground-based Granular Application	Mosquito Larvicide	0.1	5	7.73	8.2	9.6	9.8	12.0	15.2	15.8	Not Feasible
10	Low Pressure Handwand Application of 95% Liquid	Dragonfly Larvicide	0.8	5	0.12	8.2	18.5	22.0	8.5	20.5	24.8	Not Feasible
		Dragonfly Larvicide	0.8	2.5	0.23	16.3	37.0	44.0	17.0	40.9	49.6	Not Feasible
11	Backpack Application of 95% Liquid	Dragonfly Larvicide	0.8	5	No Data	3.3	4.3	4.5	4.5	6.5	6.9	Not Feasible
		Dragonfly Larvicide	0.8	2.5	No Data	6.7	8.6	9.0	9.0	13.0	13.7	Not Feasible
Flaggers												
12	Flagging For Aerial Application of Liquid Sprays	Mosquito Adulticide	0.1	7500	2.75	2.6	4.3	4.7	2.7	4.7	5.1	137.3
		Mosquito Adulticide	0.056	7500	4.90	4.7	7.8	8.4	4.9	8.3	9.1	245.1
13	Flagging For Aerial Application of Granulars	Mosquito Larvicide	0.1	800	74.79	88.4	224.4	277.8	97.2	291.7	388.9	3739.3
		Mosquito Larvicide	0.056	800	133.55	157.8	400.6	496.0	173.6	520.8	694.4	6677.4

D. Incident Data Review

A fenthion human incident review was conducted by V. Dobozy (1/30/96, D258891). Data from the national Poison Control Centers (PCCs) over the years 1985-92 reveal 52 cases of occupational exposure to fenthion and 417 cases of nonoccupational exposure, over 95% of which were due to fenthion alone. From 1993-96, PCCs reported 13 occupational exposures; of these, four had minor symptoms, one had moderate symptoms, six were seen in a health care facility, and none were hospitalized (J. Blondell, 9/29/99 e-mail). There were six reports (three involving fenthion alone) of human incidents by the California Department of Pesticide Regulation/California Pesticide Illness Surveillance Program between 1982 and 1993; of the three involving fenthion alone (one in 1982, 1983, and 1987), two resulted in systemic effects and resulted from spray blowing back in the applicator's face during mosquito treatments. The other involved a veterinary technician who spilled fenthion on her smock (1/30/96 V. Dobozy review).

VII. Aggregate Exposure and Risk Assessment

A. Acute Aggregate Exposure and Risk

The Agency is able to quantitate the food sources of dietary exposure and residential exposure; dietary exposure through drinking water has only been estimated using models. Acute dietary (food only) risks exceed the Agency's level of concern as the most exposed population subgroup, children (1-6 years), has a risk that is 800% of the aPAD (Table 3) based on moderately refined exposure estimates. Based on EECs generated via modeling, the potential exists for relatively small additional contributions to the acute aggregate risk from surface water sources of drinking water in Florida. Thus, there is concern for acute aggregate risk due to fenthion use.

B. Aggregate Short-Term and Intermediate-Term Exposures and Risks

There are food and water sources of dietary exposure as well as residential exposures to fenthion based on the current use pattern. Chronic dietary risk from food sources exceeds the Agency's level of concern with the most highly exposed population subgroup, again, being children (1-6 years) at 270% of the cPAD. Drinking water sources could possibly contribute comparatively small levels of additional dietary exposure and, hence, risk in Florida. Combined residential dermal and nondietary ingestion exposures following aerial mosquito adulticide treatments result in risks of concern to toddlers; toddler MOEs did not exceed the uncertainty factor of 100 until 2 days after application at the average application rate and until 8 days after application at the maximum application rate (risks would not be of concern using the human study as support). The Agency is, therefore, concerned about short-term and intermediate-term aggregate risk associated with the use of fenthion.

C. Chronic Aggregate Exposure and Risk

In the case of chronic aggregate risk, the Agency is able to quantitate only the food sources of dietary exposure as the drinking water residues were estimated from conservative, screening-level models. In the case of the dietary component (food only) of the chronic aggregate assessment, risks were above the Agency's level of concern with the most highly exposed population subgroup, again, being children (1-6 years) at 270% of the cPAD (Table 3); these risk values were based on moderately refined dietary exposure estimates. Again, based upon conservative modeling, the potential exists for comparatively small amounts of additional dietary exposure via drinking water. Thus, there is concern for chronic aggregate risk resulting from fenthion use.

VIII. Endocrine Disruptor Effects

EPA is required to 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..." The Agency is currently working with interested stakeholders, including other government agencies, public interest groups, industry and research scientists in developing a screening and testing program and a priority setting scheme to implement this program. When the Agency implements this program, further testing of fenthion for endocrine effects may be required.

IX. Cumulative Exposure and Risk

EPA has determined that fenthion has a common mechanism of toxicity with other members of the organophosphates. However, the Agency is in the process of developing methodology to conduct a cumulative risk assessment. For this risk assessment, therefore, EPA has not conducted a cumulative risk assessment.

X. Data Needs

The following confimatory data requirements have been identified:

A. Toxicology

- General rat metabolism
- Dominant lethal assay

B. Residue Chemistry

- Information to upgrade the ruminant and swine metabolism studies
- Recovery data for fenthion sulfoxide using FDA Multiresidue Methods
- Cattle direct animal treatment studies (ear tag and pour-on)

C. Occupational/Residential Exposure

- Data needs will be assessed during the risk mitigation process