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OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

September 10, 1999

MEMORANDUM

Subject: **ETHYL PARATHION**: Revised Human Health Risk Assessment
Chemical Number: 057501 D259500
Case Number: 0155

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Reregistration Branch 2
Health Effects Division (7509C)

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Attached is the Health Effects Division (HED) revised risk assessment for the organophosphate insecticide, ethyl parathion. This assessment summarizes the review of product and residue chemistry, toxicology, and exposure data submitted to support the reregistration of ethyl parathion and provides revised dietary and occupational risk assessments. The supporting science assessment chapters, and the 10/28/98 dietary and occupational risk assessment for ethyl parathion have been revised to reflect the receipt of comment and new data, and a reassessment of previously submitted studies.

The dietary risk assessment of 10/28/98 has been revised based on review of a new acute oral toxicity study for the animal metabolite, 4-acetamidoparaoxon. This study determined a significantly lower toxicity relative to parent parathion, and based on this study HED has excluded 4-acetamidoparaoxon from the dietary risk assessment. Occupational risk estimates have been revised to reflect a change in the dose selected for short-term risk assessment. Also, since the 10/28/98 HED risk assessment, estimates of current ethyl parathion usage have been revised by the Agency.

The following attachments provide the detailed information and conclusions on which the dietary and occupational risk assessments are based:

ETHYL PARATHION - REEVALUATION of Toxicology Endpoint Selection; Report of the Hazard Identification Assessment Review Committee (N. Paquette, 8/31/99)

Parathion. The Outcome of the HED Metabolism Assessment Review Committee Meeting Held on August 24, 1999 to Re-evaluate the Relative Toxicity of 4-Acetamidoparaoxon to Parathion (B. Cropp-Kohlligian and N. Paquette, 9/1/99)

Ethyl parathion. Product Chemistry Chapter for the Reregistration Eligibility Decision Document (K. Dockter, 8/12/99)

REVISED Residue Chemistry Chapter for the Parathion Reregistration Eligibility (RED) Document (B. Cropp-Kohlligian, 9/1/99)

Occupational and Residential Exposure Assessment and Recommendations for the Reregistration Eligibility Decision Document for Ethyl Parathion (J. Becker, 9/1/99)

Review of Parathion Incident Reports (J. Blondell, 3/30/98)

cc: RF, Reg. Std. File, R. Griffin, A. Nielsen, B. Cropp-Kohlligian, J. Becker, N. Paquette

RDI: A. Nielsen 9/9/99
CM2: Rm 712B: 703.305.5715

1.0 EXECUTIVE SUMMARY

The Health Effects Division (HED) has completed a revised human health risk assessment for the active ingredient ethyl parathion for the purpose of making a reregistration eligibility decision. Ethyl parathion, also commonly known as parathion (and referred to in this assessment as parathion), is a broad-spectrum insecticide currently registered for use on alfalfa, barley, wheat, corn (field/sweet/pop), cotton, sorghum, soybean, sunflowers, and canola. Parathion is a restricted use pesticide limited to agricultural use only.

The Agency considers the toxicological database to be adequate for reregistration and has established endpoints and doses for risk assessment based on the critical toxic effect of cholinesterase inhibition. Parathion is among the most highly toxic organophosphorus insecticides and is a potent inhibitor of acetylcholinesterase (AchE). Dose related inhibition of plasma, red blood cell (RBC) and brain cholinesterase is the critical toxic effect and occurs in dogs and rats by all routes following acute, subchronic and chronic exposures to relatively low doses.

Acute and chronic Reference Doses, established for dietary risk assessment are now termed the acute Population Adjusted Dose (aPAD) and the Chronic Population Adjusted dose (cPAD) to account for the consideration of FQPA safety factors in addition to standard uncertainty factors. HED dietary risk estimates are now expressed as a percent of the aPAD (0.00025 mg/kg body weight/day) and the cPAD (0.00003 mg/kg body weight/day).

Occupational risk, expressed as a Margin of Exposure (MOE), is based on a dose of 0.01 mg/kg bw/day for short-term exposure and 0.002 mg/kg bw/day for intermediate-term exposure. Long-term occupational exposure is not expected for ethyl parathion. No route-specific endpoint/dose has been established for inhalation exposure.

Based on the "weight-of-evidence" of all available studies, the HED Hazard Identification Assessment Review Committee (HIARC) concluded that there was no increased susceptibility to rat or rabbit fetuses following *in utero* exposure or to pups following post-natal exposure to ethyl parathion. This conclusion was confirmed by the FQPA Safety Factor Committee and the 10x safety factor was removed from risk assessment.

Product chemistry data, describing purity and physical properties, is adequate for the reregistration of the Cheminova 98% technical; additional data are required concerning UV/visible absorption. Residue chemistry data concerning metabolism, analytical methods of detection, storage stability, and magnitude of the residue in animal commodities are adequate to support reregistration. The following additional

residue chemistry data concerning magnitude of the residue in plant commodities are required: alfalfa field trial data, wheat field trial data, and soybean processing data.

Acute dietary risk estimates for the US population or US population subgroups, including infants and children, are equal to, or less than 3% of the Agency established aPAD for parathion. Chronic dietary risk estimates for the general US population, or population subgroups, are less than 1% of the cPAD. The Agency considers dietary risk estimates of less than 100 percent of the aPAD or cPAD to be below the level of concern.

Final conclusions regarding aggregate risk for parathion cannot be made at this time since the Estimated Environmental Concentration (EEC) values are greater than the Drinking Water Level of Comparison (DWLOC) values which estimate the concentration of parathion in water that, combined with the residues in food, would not be above the Agency 's level of concern. However, it should be noted that the EEC values, modeled by PRZM/EXAMS for the purposes of ecological risk assessment, are not considered accurate predictors of residue levels that may actually occur in drinking water.

The Agency considers a MOE estimate of 100 or more to be adequately protective for parathion. The occupational handler risk assessment for mixers, loaders, and applicators based on maximum Personal Protective Equipment (PPE) or engineering controls, at the application rates supported by the registrant, indicates that MOE estimates for parathion are much less than 100 for all handler scenarios (less than 1 for all scenarios) with assessment

The occupational postapplication assessment for scouts, irrigators, or other reentry workers, based on maximum PPE, indicates that entry restriction or restricted entry interval (REI) estimates range from 42 to 62 days for reentry. The interval estimates are substantially greater than the current label restricted-entry period of 3 days (6 days for sweet corn).

In the absence of exposure data, or validated modeling results, HED cannot verify that the current buffer zone of 100 feet is adequately protective to bystanders. Because the registrant is a member of the Spray Drift Task Force, HED reserves the decision concerning the magnitude of bystander spray drift exposure and the required buffer zone until data from the task force are evaluated. However, Poison Control Center data indicate that residential exposure to ethyl parathion due to spray drift does occur.

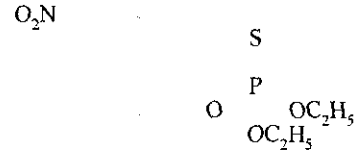
Endocrine Effects: EPA is required to develop a screening program to determine whether certain substances (including all pesticides and inerts) "may have an effect in humans that is similar to an effect produced by a naturally occurring estrogen, or such

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. EPA may require further testing of parathion for endocrine effects.

Cumulative Risk: 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/advise provided by the Science Advisory Panel. It is anticipated that this draft methodology will be available for comment and scientific review in the late summer/early fall of 1999. Consequently, the risks summarized in this document are only for parathion.

2.0 BACKGROUND

Parathion [0,0-diethyl 0-p-nitrophenyl thiophosphate] is an organophosphorus insecticide/miticide currently registered for use on alfalfa, barley, corn, cotton, canola, sorghum, soybean, sunflower, and wheat.



Empirical Formula:	$C_{10}H_{14}NO_5PS$
Molecular Weight:	291.26
CAS Registry No.:	56-38-2
PC Code:	057501

All technical parathion sold in the United States is manufactured by Cheminova Agro A/S and is formulated solely as an emulsifiable concentrate. In 1991 the Agency, and most of the registrants of products containing parathion, reached an agreement (*Federal Register Notices Vol. 56, No. 240 dated 11/13/91; and Vol. 57, No. 19 dated 1/29/92 and No. 34 dated 2/20/92)* under which the registrants agreed to limit sites and to restrict the application and postapplication practices for parathion. This action was taken by the Agency to mitigate what was considered an *unreasonable* risk to workers exposed during application and postapplication. Since the agreement, parathion use has been restricted to the crops listed above, and worker risk addressed by additional label restrictions which include; aerial-only application; mechanical-only harvesting; and other more restrictive requirements for protective clothing and handling including engineering controls.

The Biological and Economic Analysis Division (BEAD) estimates that the yearly average for total U.S. parathion use is approximately 518,000 lbs. active ingredient (a.i.), with an upper limit of approximately 872,000 lbs a.i./year (I. Yusuf and T. Kiely memo, 1/22/99). Total yearly use may vary according to pest pressure. BEAD has estimated the maximum percent of total acres, per crop, that are treated with ethyl parathion as follows: alfalfa; 1%, barley; <1%, wheat; 1%, field corn; <1%, sweet corn; <1%, cotton; <1%, sorghum; 1.5%, soybean; <1%, sunflower; 4%, and canola; 3%. Estimates of less than 1% (field/sweet corn, soybean, cotton, barley) have been rounded up to 1% for the purpose of dietary risk assessment which is based, in part, on percent crop treated estimates.

3.0 HAZARD ASSESSMENT / ENDPOINTS FOR RISK ASSESSMENT

3.1 Hazard Profile

Parathion is among the most highly toxic organophosphorus insecticides registered and is a potent inhibitor of acetylcholinesterase. Acute lethality occurs in mammals at low doses regardless of route of exposure. Toxic symptoms are largely caused by the inhibition of cholinesterase in the peripheral and central nervous system. In acute oral toxicity studies, female rats are more sensitive to the toxic and lethal effects of parathion compared to male rats.

As with all sulfur-containing organophosphates, to produce toxicity, parathion must first undergo metabolic activation to its biological active oxygen analog, paraoxon. Symptoms leading up to death are consistent with cholinergic overstimulation and include, headache, weakness, blurred vision, pin-point pupils, sweating, watering of eyes, drooling or frothing of the mouth, vomiting, tightness in the chest, labored breathing, muscle spasms, convulsions and coma. In severe poisonings, death is primarily due to respiratory arrest from paralysis of the respiratory muscles.

Dogs are the most sensitive species to cholinesterase inhibition in repeated dose studies. In subchronic and chronic studies in dogs, plasma, RBC and brain cholinesterase inhibition are the predominant critical effect occurring at relatively low doses. On the other hand, rats manifest other toxic effects, apart from the cholinergic effects. In a subchronic dietary study, female rats fed parathion also had increased mortality rates and decreased body weights and male rats had decreased body weights in addition to cholinesterase inhibition. In a chronic study, female rats had a higher mortality rate, developed anemia and retinal atrophy and degeneration and male rats developed severe myelin sheath degeneration of the sciatic nerve. These longer term toxicities occurred at doses which were greater than those lower doses which inhibited cholinesterase activity.

Parathion has been classified as a Group C (possible human carcinogen) based on increased adrenal cortical tumors in male and female Osborne-Mendel rats and possible trends for thyroid follicular adenomas and pancreatic isle cell carcinomas in male rats. However, quantified risk assessment is based on the chronic Reference Dose (cPAD) approach, which is based on non-carcinogenic effects.

Parathion is not a developmental toxicant and has no effect on reproduction. In developmental toxicity studies in rats and rabbits and a two-generation reproduction study there was no evidence of malformations or decreases in the number of pups and/or litter or surviving offspring.

The metabolism of parathion involves an oxidative desulfuration step (that

significantly enhances the anticholinesterase properties) to its oxygen analog, paraoxon. Further oxidative 0-deethylation occurs to produce hydrolysis products which are excreted almost entirely in the urine.

Table 1. Acute Toxicity / Toxicity Categories for Technical Parathion

Guideline No.	Study Type	MRIDs #	Results	Toxicity Category
870.1100	Acute Oral-Rat	243412	LD_{50} = 2.7 mg/kg, ♀ LD_{50} = 10.8 mg/kg ♂,	I
870.1200	Acute Dermal-Rabbits	Literature[1]	LD_{50} = 6.8 mg/kg	I
870.1300	Acute Inhalation	Literature[2]	LC_{50} = 0.084 mg/L	II
870.2400	Primary Eye Irritation	HED Doc # 3999	Data requirement waived I63.81-4	-
870.2500	Primary Skin Irritation	HED Doc # 3999	Data requirement waived I63.81-3	-
870.2600	Dermal Sensitization	43439110	Not a Sensitizer	-
870.6200	Acute Neurotoxicity	43117901	Neurotox: NOAEL = 2.5 mg/kg ♂ 0.5 mg/kg ♀ LOAEL = 10 mg/kg ♂ 2.5 mg/kg ♀ Based on FOB changes at 4 hours post dose	

[1] Ware, George. *The Pesticide Book,* 1989, Thomson Publication, Fresno CA. P. 305

[2] HSDB 1998. Hazard Substances Data Bank. MEDLARS online Information Retrieval System. National Library of Medicine.

3.2 Considerations for Special Sensitivity in Infants and Children (FQPA)

To address the Food Quality Protection Act (FQPA) requirement for an additional safety factor to protect infants and children, the HED Hazard Identification Assessment Review Committee (HIARC) reviewed the parathion toxicity database for evidence of neuropathology. Evidence of neuropathology may indicate an increased susceptibility of the developing nervous system to parathion. Also examined for indications of enhanced sensitivity were prenatal developmental toxicity studies in rabbits and rats, and a two-generation reproduction study in rats.

The HIARC concluded (N. Paquette memo, 3/25/98) that parathion did not demonstrate a delayed neurotoxicity in the hen or other evidence of neuropathology, except after chronic exposure and in high dosed animals. In the rabbit developmental study there were no treatment related effects on fetal weight, and no external or internal malformations observed. In the rat developmental study there were no treatment-related effects on any parameters measured on fetuses and no internal or external malformations were observed. In the two-generation reproduction study in rats there was no treatment-related reproductive toxicity in either generation throughout the study (although cholinesterase activity was not measured in offspring in this study). The HIARC also concluded that, based on the data from the developmental toxicity study in rats, a developmental neurotoxicity study with parathion is not required and there are no significant uncertainties in the assessment of functional development following pre- and/or postnatal exposure.

Based on the "weight-of-evidence" of all available studies, the HIARC concluded that there was no increased susceptibility to rat or rabbit fetuses following *in utero* exposure or to pups following post-natal exposure to parathion. Based on the data summarized above, the Committee recommended in the *Comprehensive Review of the Organophosphates* (June 4, 1998) that the 10x FQPA safety factor be reduced to 1x for the calculations of both the aPAD and cPAD (the population adjusted dose is based on the standard Reference Dose RfD with amendment to account for decisions considering FQPA). This recommendation was confirmed in HED's *Combined Report of the HIARC and Safety Factor Committee and its Recommendations for the Organophosphates* (August 6, 1998).

3.3 Carcinogenicity

In 1991, the HED Carcinogenicity Peer Review Committee reevaluated the carcinogenic classification of parathion. Parathion has been classified as a Group C (possible human carcinogen) based on increased adrenal cortical tumors in male and female Osborne-Mendel rats and possible trends for thyroid follicular adenomas and pancreatic isle cell carcinomas in male rats. The Committee recommended that

quantified risk assessment be based on the chronic Reference Dose, (now termed cPAD), which is based on non-carcinogenic effects. The RfD (cPAD) approach will adequately account for chronic toxicity effects, including carcinogenicity, since doses eliciting cholinesterase inhibition are significantly below those eliciting the carcinogenic effects summarized above.

3.4 Endpoint / Dose Selection for Dietary Risk Assessment

Acute Population Adjusted Dose (aPAD)

The Agency has established an acute Population Adjusted Dose (aPAD) of 0.0003 mg/kg body weight(bw)/day to assess the risk associated with a single oral exposure to parathion. The aPAD is based on plasma and RBC cholinesterase inhibition demonstrated in male rats in an acute neurotoxicity study. In this study neurobehavioral and neuropathological effects, plasma, RBC, and brain cholinesterase were determined. This study is appropriate for use in acute dietary risk assessment since the endpoint of cholinesterase inhibition was measured 4 hours after a single oral dose (exposure period of concern) on the day of treatment.

Based on the results of this study, male rats had plasma and RBC cholinesterase inhibition at 2.5 mg/kg (LOAEL) with a NOAEL of 0.025 mg/kg. In female rats, plasma and RBC cholinesterase was inhibited at 2.5 mg/kg (LOAEL) with a NOAEL of 0.5 mg/kg. The neurobehavioral NOAEL is 2.5 mg/kg for males and 0.5 mg/kg for females, with abnormal functional observational battery (FOB) and clinical signs of cholinergic toxicity evidenced at the LOAEL of 10 mg/kg for males and 2.5 mg/kg for females. The brain cholinesterse inhibition LOAEL was 10 mg/kg for males and 2.5 mg/kg for females.

The aPAD for parathion (0.00025 mg/kg bw/day) is based on the dose of 0.025 mg/kg bw/day (NOAEL) and combined Uncertainty Factors of 10x for interspecies extrapolation, 10x for intraspecies variability, and 1x to account for FQPA considerations.

Chronic Population Adjusted Dose (cPAD)

The Agency has established a chronic Population Adjusted Dose (cPAD) of 0.00003 mg/kg bw/day to assess the risk associated with long-term (one-year or more) dietary exposure to parathion. The cPAD is based on plasma and RBC cholinesterase inhibition observed in a one-year feeding study in dogs. Dose-related decreases in plasma and RBC cholinesterase activity were observed at all dose levels in both male and female dogs. Brain cholinesterase was statistically significantly reduced only in mid-dose group females. The LOAEL was 0.01 mg/kg bw/day (lowest dose tested, or LDT) based on decreased plasma and RBC cholinesterase in both males and females.

A NOAEL for plasma/RBC cholinesterase inhibition was not established in this study.

The cPAD for parathion (0.00003 mg/kg bw/day) is based on the dose of 0.01 mg/kg bw/day and Uncertainty Factors of 10x for interspecies extrapolation, 10x for intraspecies variability, 3x for the lack of a NOAEL, and 1x to account for FQPA considerations.

3.5 Endpoint / Dose Selection for Occupational Risk Assessment

Inhalation and Dermal Absorption

HED has based the parathion occupational risk assessment on an estimate that 100 percent absorption occurs in the dermal and inhalation route of exposure. This estimate is supported by the oral LD_{50}, dermal LD_{50}, and inhalation LC_{50} studies which demonstrated toxicity at similar doses in multiple species *via* all routes of exposure.

Inhalation Exposure

Due to the known acute toxicity of parathion, in 1985 the Agency waived the requirement for an inhalation toxicity study. No inhalation-specific endpoint has been established for parathion. However, based on the high acute toxicity shown in a rat study (LC_{50}=0.084 mg/L), and use patterns of up to 1 lb. active ingredient/acre, there is considerable concern for occupational inhalation exposure to parathion. Inhalation of parathion vapor or aerosol leads to rapid absorption with imminent risk of respiratory failure. The HIARC concluded that inhalation exposure estimates should be converted to an equivalent of an oral dose (in mg/kg bw/day), aggregated with the dermal exposure estimate (also converted to an oral equivalent) and the resulting sum compared to the short and/or intermediate (oral) doses designated for occupational risk assessment.

Short-Term (1-7 Day) Exposure

Due to the known acute toxicity of parathion, in 1985 the Agency waived the requirement for a dermal toxicity study. No dermal-specific endpoint has been established for parathion risk assessment.

The occupational risk assessment for short-term, combined dermal and inhalation exposure to parathion, is based on the dose (NOAEL) of 0.01 mg/kg body weight/day established in a six-month dog *oral* toxicity study. This study demonstrated decreased plasma cholinesterase in males and females (84 and 79%, respectively) at 0.8 mg/kg bw/day (LOAEL), measured at the *one-week* time period. No other subchronic rat or dog study was available that measured cholinesterase activity at the one-week time period.

Exposure estimates are compared to the dose level of 0.01 mg/kg bw/day and risk is expressed as a margin of exposure (the ratio of estimated exposure to 0.01 mg/kg bw/day). The Agency considers Margin of Exposure (MOE) estimates of 100 or greater (based on 10x for interspecies extrapolation and 10x for intraspecies variability) to be adequately protective for short-term exposure to parathion.

Intermediate-Term (>7 Day to Several Months) Exposure

The risk assessment for intermediate-term, combined dermal and inhalation occupational exposure to parathion, is based on the dose (NOAEL) of 0.0024 mg/kg bw/day established in the 6-month *oral* toxicity study in dogs which demonstrated markedly reduced plasma cholinesterase in both males and females observed by Week 6 and throughout the study at 0.08 mg/kg bw/day (study LOAEL). Exposure estimates are compared to the dose level of 0.002 mg/kg bw/day and risk is expressed as a margin of exposure. The Agency considers MOE estimates of 100 or greater to be adequately protective for intermediate-term exposure to parathion.

Long-Term Exposure

The HIARC concluded that, based on current use patterns for parathion there is likely no worker exposure of the duration considered long-term (several months of continuous exposure) and risk assessment for this duration is not required. No endpoint/dose was established for risk assessment.

Table 2. Summary of Toxicology Endpoint Selection

EXPOSURE SCENARIO	DOSE (mg/kg/day)	ENDPOINT	STUDY
Acute Dietary	NOAEL=0.025 UF = 100	Plasma and RBC ChE Inhibition in males at 2.5 mg/kg	Acute Oral Neurotoxicity in Rats
	Acute PAD = 0.00025 mg/kg/day		
Chronic Dietary	LOAEL=0.01 UF = 300	Plasma and RBC ChE Inhibition in both male and female dogs at 0.1 mg/kg bw/day	Chronic Toxicity in Dogs
	Chronic PAD = 0.00003 mg/kg/day		
Short-Term (Dermal)	Oral NOAEL=0.01 UF = 100	Plasma ChE Inhibition in male and female dogs after 1 week of dosing at 0.8 mg/kg bw/day	6-Month Oral Toxicity Study in Dogs
Intermediate-Term (Dermal)	Oral NOAEL=0.002 UF = 100	Plasma and RBC ChE Inhibition in both male and female dogs at 0.008 (0.01) mg/kg bw/day	6-Month Oral Toxicity Study in Dogs
Long-Term (Dermal)	The use pattern and exposure scenario does not indicate a need for long-term risk assessment		
Short-Term (Inhalation)	Oral NOAEL=0.01 UF = 100	Plasma ChE Inhibition in male and female dogs after 1 week of dosing at 0.8 mg/kg bw/day	6-Month Oral Toxicity Study in Dogs
Intermediate-Term (Inhalation)	Oral NOAEL=0.002 UF = 100	Plasma and RBC ChE Inhibition in both male and female dogs at 0.008 (0.01) mg/kg bw/day	6-Month Oral Toxicity Study in Dogs
Long-Term (Inhalation)	The use pattern and exposure scenario does not indicate a need for long-term risk assessment		

4.0 DIETARY EXPOSURE / FOOD USES

4.1 Residue Profile

On 3/11/98 the HED Metabolism Assessment Review Committee (memo by B. Cropp-Kohlligian, 5/21/98) met to discuss the available parathion plant and animal metabolism data (animal magnitude of the residue data were not available) and concluded the following. Parathion residues of concern in plant commodities include

parathion, its metabolite paraoxon [O,O-diethyl-O-p-nitrophenyl phosphate], and p-nitrophenol and that parathion residues of concern in animal commodities include parathion, paraoxon, *p*-nitrophenol, and 4-acetamidoparaoxon. The tolerance expression for plant and animal commodities should be based on parathion only. Parathion residues of concern to be included in the risk assessment for plant commodities with regard to cholinesterase inhibition should include parathion and paraoxon. Parathion residues of concern to be included in the risk assessment for animal commodities with regard to cholinesterase inhibition should include parathion, paraoxon, and 4-acetamidoparaoxon. Residues of *p*-nitrophenol resulting from the use of parathion do not have to be included in the tolerance expression or considered in the aggregate risk assessment for parathion with regard to cholinesterase inhibition.

At that same meeting, the HED Metabolism Assessment Review Committee (memo by B. Cropp-Kohlligian dated 5/21/98) further concluded, as had an earlier HED Metabolism Committee (memo by S. Hummel dated 2/10/95), that if the registrant could demonstrate that 4-acetamidoparaoxon is much less toxic than parathion by providing acute oral toxicity data demonstrating that the LD_{50} for 4-acetamidoparaoxon is more than 200 mg/kg, then 4-acetamidoparaoxon residues incurred in animal commodities would not need to be included in the dietary risk assessment for parathion.

Subsequently, the registrant (Cheminova) submitted acute oral toxicity data to address the Agency's concerns regarding the toxicity of 4-acetamidoparaoxon as well as animal magnitude of the residue data. Based on the "weight-of-evidence" demonstrating that 4-acetamidoparaoxon was significantly less acutely toxic than parathion, the HED Metabolism Review Committee concluded that residues of 4-acetamidoparaoxon incurred in animal commodities resulting from exposure of livestock to residues of parathion in/on feed items does not have to be included in the dietary risk assessment for parathion with regard to cholinesterase inhibition. The Committee noted that although 4-acetamidoparaoxon comprises most of the total residue in milk, the dietary risk is not significant when the lower toxicity and estimated residue level (1 ppb) of that metabolite are taken into account.

The HED Metabolism Assessment Review Committee (B. Cropp-Kohlligian memo, 5/21/98 and B. Cropp-Kohlligian, N. Paquette memo, 9/1/99) has concluded that parathion residues of concern in plant and animal commodities include parathion, its metabolite paraoxon [*O,O*-diethyl-*O*-*p*-nitrophenyl phosphate], and *p*-nitrophenol. Residues of concern to be included in the risk assessment for plant and animal commodities will include parathion and paraoxon. Residues of *p*-nitrophenol resulting from the use of parathion do not need to be included in the tolerance expression or considered in the aggregate risk assessment for parathion.

Tolerances for residues of parathion or its methyl homolog (methyl parathion) in/on numerous raw agricultural commodities (RACs) have been established under 40

CFR §180.121(a) and §180.319. No tolerances for residues of parathion have been established for animal commodities or processed food/feed commodities. Although tolerances for residues of parathion are currently expressed in terms of parathion or its methyl homolog (methyl parathion) [40 CFR §180.121 (a) and §180.319], the Agency has recommended that tolerances for parathion should be moved from 40 CFR §180.121(a) and listed under a separate 40 CFR §180.XXX (a) section. Under the new listing, tolerances should only be established for RACs and, if necessary, processed commodities of alfalfa, barley, canola, corn, cotton, grain sorghum, soybean, sunflower, and wheat, in accordance with an agreement limiting the use of parathion to these crops. All other currently established tolerances for residues of parathion listed under 40 CFR §180.121 (a) and §180.319 should be revoked.

The tolerance expression for plant and animal commodities will be based on parathion *only*. The tolerance definition for parathion residues should also be changed to read as follows; "Tolerances are established for the residues of parathion [O,O-diethyl-O-p-nitrophenyl thiophosphate] in/on the following raw agricultural commodities:"

> *In their responses to the Agency's Preliminary Human Risk Assessment of Parathion, the registrant (Cheminova) has made it clear to the Agency that they will only support the food/feed uses of parathion specified under our agreement. At this time, no other party has committed to support any other use of parathion. Hence, the Residue Chemistry Science Assessments and Tolerance Reassessment Summary only include recommendations for commodities of the food/feed crops specified under the "Agreement" referred to above. If the Agency determines that other uses of parathion and/or tolerances for residues of parathion must be retained, additional residue chemistry data may be required to support the reregistration of parathion.*

4.2 Directions for Use

All conclusions regarding the adequacy of residue chemistry data to satisfy reregistration requirements for parathion are predicated on the use sites, maximum use patterns, and restrictions of parathion summarized in the table below.

Table 3. Label Rates / Use Patterns

Crop	Maximum Single Application Rate (ai)	Max. # Apps.[a]	Minimum Retreatment Interval (Days)	Pre-Harvest Interval (Days)
Alfalfa (grown for forage and hay only)	0.50 lb/A	2 per cutting	7	15
Barley	0.75 lb/A	6	7	15
Canola	0.50 lb/A	2	7	28
Corn, field/pop/sweet	0.75 lb/A	6	7	12
Cotton	1.0 lb/A	6	7	7
Sorghum, grain only	1.0 lb/A	2	7	12-forage 28-grain 28-stover
Soybeans [b]	0.75 lb/A	2	7	20
Sunflowers	1.0 lb/A	3	5	30
Wheat	0.50 lb/A	2	14	15

[a] Maximum number of applications at the maximum single application rate.

[b] The following restrictive language is required: Do not feed green immature growing plants to livestock. Do not harvest for livestock feed

4.3 Nature of the Residue in Plants / Animals

The qualitative nature of the residue in plants and animals is adequately understood based on acceptable cotton, potato, wheat, ruminant, and poultry metabolism studies. Parathion residues of concern in plant and animal commodities are parathion, paraoxon, and p-nitrophenol.

4.4 Residue Analytical Methods

Adequate analytical methodology is available for data collection and for the enforcement of parathion tolerances as currently defined. The Pesticide Analytical Manual (PAM) Vol. II lists methods I(a) and I(b)(PAM, Vol. I multiresidue methods for organophosphates), and I(c) and I(d) for parathion.

The registrant has proposed new enforcement methods for plant and animal commodities using GC/FPD. These methods have been successfully radiovalidated using samples from the plant and animal metabolism studies. The proposed enforcement method for plant commodities has been successfully validated using samples of representative plant commodities by both an independent laboratory and by the Agency; the limit of quantitation (LOQ) for residues of parathion in plant commodities is 0.04 ppm. The registrant (Cheminova) has submitted independent laboratory validation (ILV) data for the proposed enforcement method for animal commodities which are under review. Pending acceptance of these data to satisfy guideline requirements, no additional animal residue analytical methods data are required of the registrant to support the reregistration of parathion. A method validation study will be conducted by the Agency, as the Agency deems appropriate, determining residues of parathion and possibly residues of paraoxon and 4-acetamidoparaoxon in egg and poultry tissues (at the LOQ for each analyte; 0.001 ppm and 0.01 ppm, respectively). FDA multiresidue methods provide complete recovery of residues of parathion and paraoxon.

4.5 Storage Stability Data

For purposes of reregistration, the requirements for supporting storage stability data are satisfied for all acceptable residue studies. Generally, residues of parathion and paraoxon are stable in most crop matrices for at least 2 years. The registrant (Cheminova) has submitted new storage stability data on field corn grain, meal, grits, flour, starch, and refined oil and test sample storage intervals/conditions information from magnitude of the residue studies which are under review.

4.6 Magnitude of the Residue / Plants

In support of the reregistration of the EC formulations of parathion the registrant (Cheminova) has submitted the following new residue chemistry data which are under review: (i) barley grain, hay, and straw magnitude of the residue data, (ii) magnitude of the residue data on aspirated grain fractions (AGF) derived from wheat grain and sorghum grain, and (iii) cotton gin trash magnitude of the residue data. Pending acceptance of these data to fulfill guideline requirements and provided the registrants amend all end-use product labels, as necessary, to conform to the food/feed use sites, maximum use patterns, and restrictions as specified in the table above, no additional magnitude of the residue data are required to support the reregistration of parathion on barley, canola, corn, cotton, grain sorghum, soybeans, and wheat except wheat hay. Additional magnitude of the residue data are required on the following commodities: alfalfa forage, alfalfa hay, and wheat hay. The wheat hay data are considered confirmatory; however, since it is unlikely that the currently established tolerances for residues of parathion in/on alfalfa forage and alfalfa hay are adequate, these required data are considered critical to tolerance reassessment. The registrant has committed to generate the subject alfalfa data.

4.7 Magnitude of the Residue / Processed Commodites

Reregistration requirements for magnitude of the residue in processed food/feed commodities are fulfilled for canola seed, field corn grain, cottonseed, sunflower seed, wheat grain, and barley grain (tranlated from wheat grain). Data demonstrating the potential for concentration of parathion residues of concern in soybean processed commodities is required. These data are considered confirmatory.

4.8 Magnitude of the Residue in Meat, Milk, Poultry, and Eggs

The available ruminant and poultry feeding studies are adequate to support the reregistration of parathion. No additional meat, milk, poultry, and egg magnitude of the residue data are required. No tolerances for residues of parathion in milk and meat are required; however, tolerances for residues of parathion, set at the LOQs of the enforcement method, should be established in eggs, and poultry muscle, fat, and liver. A tolerance level of 1 ppb or 0.001 ppm would be appropriate for egg and 10 ppb or 0.01 ppm would be appropriate for poultry muscle, poultry fat, and poultry liver.

4.9 Confined Accumulation in Rotational Crops

The registrant (Cheminova) has submitted confined rotation crop data, which are under review. Pending acceptance of these data to satisfy guideline requirements, no additional confined rotational crop data are required to support the reregistration of parathion.

5.0 DIETARY RISK ASSESSMENT

5.1 Residue Estimates for Risk Assessment

The dietary exposure estimates for residues of parathion and paraoxon in/on crop commodities used in the acute and chronic dietary risk assessments are based on available Food and Drug Administration (FDA) and Pesticide Data Program (PDP) monitoring data for corn (grain and sweet), soybeans, and wheat grain (translated to barley grain), available field trial data for canola seed, cottonseed, grain sorghum, and sunflower seed, and available processing data for canola seed, field corn grain, cottonseed, sunflower seed, and wheat grain. Since the most recent Qualitative Usage Analysis (QUA) report for parathion (I. Yusuf and T. Kiely memo, dated 1/22/99) predicts that extremely low percentages of barley, corn, soybeans, and wheat acres planted will be treated with parathion (<1% maximum for each of these crops), percent crop treated data have been incorporated into all dietary exposure estimates for crop commodities used in the acute and chronic dietary risk assessments.

The dietary exposure estimates for residues of parathion and paraoxon in animal commodities (egg and poultry tissues) used in the acute and chronic dietary risk assessments are based on available poultry magnitude of the residue data. Percent crop treated data were

also used in the poultry dietary burden calculation for the dietary exposure estimates for egg and poultry tissues used in the chronic dietary risk assessment. [Note: Since there is no reasonable expectation of finite residues of parathion and paraoxon in milk and ruminant tissues, dietary exposure estimates for residues of parathion and paraoxon in these animal commodities are zero.]

Table 4. Residue Data Summary

Commodity [a]	Processing Factor To Be Used In Chronic and Acute Assessments	Source of Data for Assessment (PDP, FDA, Field Trial, etc.)	Anticipated Residue Estimate Entered into Chronic Risk Assessment	Anticipated Residue Estimate Entered into Acute Risk Assessment
Barley grain, all forms	DEEM Default = 1	Translated from wheat grain which is based on 1994-1998 FDA Monitoring Data.	***Translated from wheat grain. See wheat grain.***	
Corn grain, sugar/hfcs	Reset DEEM Default to 1	1994-1998 FDA Monitoring Data for whole grain corn (field and popped)	Parathion Residues (Ave.) = 0.0015 ppm Paraoxon Residues = zero 1% Crop Treated **Anticipated Residue Estimate = 0.000015 ppm**	
Corn grain, endosperm, all forms	DEEM Default = 1			
Corn grain, bran, all forms	DEEM Default = 1			
Corn grain, oil	Processing Data Refined oil = 1.9			
Corn grain, sugar/molasses	DEEM Default = 1.5			
Corn grain, popped, all forms	DEEM Default = 1			
Corn sweet, all forms	DEEM Default = 1	1994-1998 FDA Monitoring Data for sweet corn	Parathion Residues (Ave.)=0.0015ppm Paraoxon Residues = zero 1% Crop Treated **Anticipated Residue Estimate=0.000015 ppm**	**RDF#1** **TotalNZ=1@0.0015 ppm** **TotalZ=99**
Cottonseed, meal	Processing Data Meal = 0.02x	Cottonseed Field Trial Data	Parathion Residues (Ave.) = 0.45 ppm Paraoxon Residues = zero 1% Crop Treated **Anticipated Residue Estimate = 0.0045 ppm**	
Cottonseed, oil	Processing Data Refined oil = 0.02x			
Canola, oil	Processing Data Refined oil = 1.5	Canola seed Field Trial Data	Parathion Residues (Ave.) = 0.07 ppm Paraoxon Residues (Ave.) = 0.0075 ppm 3% Crop Treated **Anticipated Residue Estimate = 0.0023 ppm**	

Commodity [a]	Processing Factor To Be Used In Chronic and Acute Assessments	Source of Data for Assessment (PDP, FDA, Field Trial, etc.)	Anticipated Residue Estimate Entered into Chronic Risk Assessment	Anticipated Residue Estimate Entered into Acute Risk Assessment
Sorghum, grain	DEEM Default = 1	Sorghum Grain Field Trial Data	Parathion Residues (Ave.) = 0.68 ppm Paraoxon Residues (Ave.) = 0.05 ppm 1% Crop Treated **Anticipated Residue Estimate = 0.0073 ppm**	
Soybeans, mature seeds dry, all forms	DEEM Default = 1	1994-1998 FDA Monitoring Data supported by 1997-1998 PDP Monitoring Data for soybeans	Parathion Residues (Ave.) = 0.0015 ppm Paraoxon Residues = zero 1% Crop Treated **Anticipated Residue Estimate = 0.000015 ppm**	
Soybean, sprouted seeds	DEEM Default = 0.33			
Soybean, flour, all forms	DEEM Default = 1			
Soybean, protein isolate, all forms	DEEM Default = 1			
Soybean, oil	DEEM Default = 1			
Sunflower seeds	DEEM Default = 1	Sunflower seed Field Trial Data	Parathion Residues (Ave.) = 0.025 ppm Paraoxon Residues (Ave.) = 0.025 ppm 4% Crop Treated **Anticipated Residue Estimate = 0.002 ppm**	
Sunflower seed oil	Processing Data Refined Oil = 0.44			
Wheat grain, rough, all forms	DEEM Default = 1	1994-1998 FDA Monitoring Data supported by the 1995-1997 PDP Monitoring Data on wheat grain	Parathion Residues (Ave.) = 0.0015 ppm Paraoxon Residues (Ave.) = 0.0015 ppm 1% Crop Treated **Anticipated Residue Estimate = 0.00003 ppm**	
Wheat grain, germ, all forms	DEEM Default = 1			
Wheat grain, bran, all forms	Processing Data Wheat bran = 4.6			
Wheat grain, flour, all forms	Processing Data Wheat flour = 0.4			
Wheat grain, germ oil	DEEM Default = 1			

Commodity [a]	Processing Factor To Be Used In Chronic and Acute Assessments	Source of Data for Assessment (PDP, FDA, Field Trial, etc.)	Anticipated Residue Estimate Entered into Chronic Risk Assessment	Anticipated Residue Estimate Entered into Acute Risk Assessment
Egg and Poultry Tissues	DEEM Default = 1	Livestock feeding studies and field trial data	Average residues of parathion (w/paraoxon estimated at zero) and based on 1% barley treated with parathion at the maximum use rate: **Egg = 0.000001 ppm (rounded)** **Muscle = 0.000001 ppm (rounded)** **Fat = 0.000004 ppm** **Liver = 0.000005 ppm**	Average residues of parathion (w/paraoxon estimated at zero) and based on 100% barley treated with parathion at the maximum use rate: **Egg = 0.00007 ppm** **Muscle = 0.00005 ppm** **Fat = 0.0004 ppm** **Liver = 0.0005 ppm**

[a] All plant commodities are considered Blended except sweet corn which is considered Not Blended and sunflower seed which is considered Partially Blended

5.2 Dietary Risk Estimates

Deem Program / Consumption Data

The Agency is currently using software developed by Novigen Sciences, Inc., named the *Dietary Exposure Evaluation Model*, or DEEM™ , to calculate acute and chronic dietary risk estimates for the general U.S. population and defined population subgroups, including infants and children. Food consumption data used in the program is based on the *USDA Continuing Survey of Food Intake by Individuals* (CSFII). The Agency is currently using the CSFII 1989-92 consumption data, which is based on the reported food consumption of 10,383 individuals over a 3 day interval. Foods "as eaten" (such as cherry pie) are linked to Raw Agricultural Commodities (RACs) such as cherries, wheat, oil, etc. by the use of "recipe" translation files based on USDA data.

For chronic dietary risk assessment, consumption data are averaged for the entire U.S. population, and within population subgroups such as "all infants". The averaged consumption estimate of each population group is multiplied by an averaged residue estimate, based on field trial and/or monitoring data (PDP/FDA), for each crop (apples) or processed commodity (apple-juice) of interest. Chronic dietary exposure estimates are calculated by the DEEM program in mg/kg body weight/day and dietary risk is calculated as a percent of the cPAD.

Acute dietary exposure estimates are not based on averaged consumption data.

Instead, 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. A dietary exposure distribution based on point estimates for residues in foods is termed "deterministic", and can be used to estimate an upper-bound for acute risk. A more refined probabilistic (Monte Carlo) type acute exposure estimate can be made if appropriate residue data (a distribution of residue in foods of interest) is available. Probabilistic exposure estimates also typically incorporate percent crop treated data to reflect the probability that a commodity has zero residue due to non-treatment. Acute dietary exposure estimates are calculated by the DEEM program in mg/kg body weight/day and risk is calculated as a percent of the aPAD.

Acute Dietary Risk Estimates

The DEEM model was used to calculate acute dietary exposure estimates based on *total single-day* (rather than single-serving) consumption data. Based on the residue and consumption data outlined above, the DEEM program estimates that the "U.S. population - all seasons" and all population subgroups, including infants and children, are acutely (at maximum) exposed to parathion at a level equal to or less than 3% (at the 99.9% exposure level) of the aPAD. HED refers to the 99.9% exposure level for this risk assessment based on the high level of refinement.

Table 5. Acute Dietary Exposure and Risk Estimates

Population Subgroup	95th Percentile		99th Percentile		99.9th Percentile	
	Exposure (mg/kg/d)	%aPAD[a]	Exposure (mg/kg/d)	%aPAD[a]	Exposure (mg/kg/d)	%aPAD[a]
U.S. Population	0.0000004	0.2	0.000001	0.4	0.000003	1
Non-nursing Infants	0.0000005	0.2	0.000001	0.5	0.000004	2
Children 1-6	0.0000010	0.4	0.000002	0.6	0.000007	3
Children 7-12	0.0000010	0.3	0.000001	0.5	0.000004	2
Females 13-19	0.0000004	0.2	0.000001	0.6	0.000002	1
Males 13-19	0.0000004	0.2	0.000001	0.4	0.000003	2
Females 20+	0.0000003	0.1	0.000001	0.2	0.000002	1
Males 20+	0.0000003	0.2	0.000001	0.3	0.000002	1

[a] The aPAD is 0.00025 mg/kg bw/day for all population subgroups.

Chronic Dietary Risk Estimates

The DEEM model was used to calculate chronic dietary exposure estimates based on *average* consumption data for the US population and population subgroups including infants and children. Based on the residue and percent crop treated data outlined above, the DEEM program estimates that the "U.S. population - all seasons" and all population subgroups, including infants and children, are chronically exposed to parathion at a level less than 1% of the chronic Population Adjusted Dose.

Table 6. Chronic Dietary Exposure and Risk Estimates

Population Subgroup	Exposure (mg/kg bw/day)	Percent of Chronic PAD [a]
U.S. Population	<0.000001	0.2
Non-nursing Infants <1 year	<0.000001	0.3
Children 1-6	<0.000001	0.5
Children 7-12	<0.000001	0.4
Females 13-19	<0.000001	0.3
Males 13-19	<0.000001	0.3
Females 20+	<0.000001	0.2
Males 20+	<0.000001	0.2

[a] The cPAD is 0.00003 mg/kg bw/day for all population subgroups.

6.0 DRINKING WATER EXPOSURE AND RISK

HED uses Drinking Water Levels of Comparison (DWLOCs) values as a surrogate measure of exposure. The models currently used to estimate pesticide concentrations in drinking water are very conservative and used as screening tools in the risk assessment process. We do not use the current model estimates from GENEEC, PRZM/EXAMS and SCI-GROW to quantify exposure and risk as a %RfD (% of the reference dose) or %PAD (% of the population adjusted dose). Instead, we compare the model estimates to DWLOC values. This comparison provides a semi-quantitative risk assessment for drinking water until monitoring data can be obtained.

In calculating a DWLOC, we determine how much of the acceptable exposure (i.e., the RfD or PAD) is available for exposure through drinking water. Simply, if 10 mg/kg/day is the chronic RfD or PAD, and chronic exposure through average food residues is 6 mg/kg/day, and there are no residential uses, and therefore no residential exposures, then 4 mg/kg/day is "allowed" for exposure through drinking water. This allowable exposure through drinking water is used to calculate a *theoretical* concentration limit for the pesticide in drinking water.

In general, the $DWLOC_{ACUTE}$ is the concentration in drinking water as a part of the aggregate acute exposure that occupies no more than 100% of the acute RfD or aPAD. The $DWLOC_{CHRONIC}$ is the concentration in drinking water as a part of the aggregate chronic exposure that occupies no more than 100% of the chronic RfD or cPAD. The Agency's standard body weights and water consumption values used to calculate DWLOCs are as

follows: 70kg and 2L/day (adult male), 60 kg and 2L/day (adult female), and 10 kg and 1L/day (child). To calculate chronic and acute DWLOC values, the chronic and acute dietary food exposure was subtracted from the cPAD and aPAD, respectively, using the equation:

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

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

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

The results are summarized below.

Table 7. DWLOC Estimates

Acute

Population	EECS Based on PRZM / EXAMS (ug/L)	Acute PAD	Acute Food Exposure (mg/kg/day)	Water Exposure (mg/kg/day)	$DWLOC_{acute}$ (μg/L)
Adult Male	4.7 (alfalfa) - 60.9 (sorghum)	0.00025	0.000003	0.000247	9
Adult Female	4.7 (alfalfa) - 60.9 (sorghum)	0.00025	0.000002	0.000248	7
Infants <1 yr	4.7 (alfalfa) - 60.9 (sorghum)	0.00025	0.000004	0.000246	2
Children 1-6	4.7 (alfalfa) - 60.9 (sorghum)	0.00025	0.000007	0.000243	2
Children 7-12	4.7 (alfalfa) - 60.9 (sorghum)	0.00025	0.000004	0.000246	2

Chronic

Population	EECS Based on PRZM-EXAMS (ug/L)	Chronic PAD (mg/kg/day)	Chronic Food Exposure (mg/kg/day)	Chronic H_2O Exposure (mg/kg/day)	$DWLOC_{chronic}$ (ug/L)
Adult Male	0.6 (alfalfa) - 5.4 (sorghum)	0.00003	0.0000001	0.000030	1
Adult Female	0.6 (alfalfa) - 5.4 (sorghum)	0.00003	0.0000001	0.000030	1
Infants <1 yr	0.6 (alfalfa) - 5.4 (sorghum)	0.00003	0.0000001	0.000030	0.3
Children 1-6	0.6 (alfalfa) - 5.4 (sorghum)	0.00003	0.0000002	0.000030	0.3
Children 7-12	0.6 (alfalfa) - 5.4 (sorghum)	0.00003	0.0000001	0.000030	0.3

The EEC values in the above table, based on PRZM-EXAMS modeling, are greater than the estimated DWLOC for all population groups, and for both acute and chronic exposure.

7.0 RESIDENTIAL EXPOSURE / RISK

Parathion is a restricted use pesticide limited to agricultural use *only*. There are no labeled residential uses.

All labels include language concerning the maintenance of a buffer zone of 100 feet from buildings, public roads, or bodies of water to minimize the exposure *via* spray drift to bystanders. However, data indicates that ethyl parathion residential exposure may result from spray drift due to aerial application to adjacent agricultural fields. HED has not quantitatively assessed the exposure to individuals living adjacent to agricultural land. Methods to assess these risks are currently being developed by the Agency, and these assessments will be conducted in the future when these methods are available. The Agency remains concerned that the existing buffer zones may not be not adequately protective and would not prevent ethyl parathion exposure to bystanders. The Agency reserves decisions concerning the magnitude of bystander spray drift exposure and the required buffer zone until data from the Spray Drift Task Force (of which Cheminova is a member) are fully evaluated.

8.0 AGGREGATE DIETARY EXPOSURE AND RISK

Final conclusions regarding aggregate risk for parathion cannot be made at this time since the drinking water EEC values (above) are greater than the DWLOC values derived from food use exposure estimates. However, it should be noted that EEC values, modeled by PRZM/EXAMS for the purposes of ecological risk assessment, are not considered accurate predictors of residue levels that may actually occur in drinking water.

9.0 OCCUPATIONAL EXPOSURE AND RISK

9.1 Background / Restrictions

The agreement of 12/13/91, which limited the use of parathion to nine crops (alfalfa, barley, canola, corn, cotton, soybeans, sorghum, sunflower, and wheat), also increased parathion handling and postapplication restrictions to reduce worker exposure.

Handler restrictions include: 1) mixers/loaders must use a closed mixing system; 2) liquid parathion must be removed from its original shipping container and transferred to the mixing tank using hoses equipped with a dry-couple shut-off device that will minimize drips to not more than 2 milliliters per disconnect; 3) an observer must be present during all mixing/loading activities in order to assist in the event of an accident; 4) the only application method permitted is by aircraft (by certified commercial applicators); 5) human flaggers are strictly prohibited; and 6) pilots may not apply parathion if they have earlier in the day performed any mixing/loading activities.

Postapplication restrictions include: 1) a crop that has been treated with parathion must

be harvested by mechanical means only; 2) no reentry is allow under any circumstances for the first 4 hours following the end of the application; and 3) current labels state the restricted-entry period is 3 days (6 days for corn); entry into the entry-restricted areas during this time is limited to workers scouting and irrigating the crop who must wear PPE consisting of coveralls over long-sleeved shirts and long pants, chemical resistant boots, and chemical resistant gloves.

9.2 Incident Data

Based on a recent review (J. Blondell memo, 3/30/98) of parathion poisoning data following the consent agreement (1992-1996), the following poisoning incidents have been reported: 1) incident data system (IDS) includes two incidents, one from Minnesota and one from South Dakota and both were related to spray drift exposure. Systemic / health effects were not reported; 2) California reported six incidents involving ethyl parathion in 1992, and no incidents from 1993 through 1996. Three incidents involved drift from a plum orchard related to misuse. The three other incidents related to handlers cleaning or working on spray rig; and 3) Poison Control Center data from 1993 through1996 report 72 cases of parathion exposures. Thirty-four cases were followed to determine outcome, 13 cases with minor medical outcome and 4 cases with moderate outcome. It appears that most of these cases involve spray drift, given that they occur in a residence and generally involve environmental residues. A very small number of parathion cases have been reported since the settlement agreement in 1991. In most cases the existence of health effects, if any, is not documented. For the incidents that are reported, either spray drift or equipment maintenance are the principle sources of exposure.

9.3 Handler Exposure

Scenarios for Risk Assessment

HED has identified three major handler exposure scenarios: (1) mixing / loading liquids for aerial application; (2) applying sprays with fixed-wing aircraft; and (3) applying sprays with helicopters (PHED data for helicopter application of sprays are based on a very limited number of replicates. Instead of assessing this exposure scenario using inadequate data, data from PHED for fixed-wing application of sprays were used in accordance with HED Science Advisory Council for Exposure Policy Number 5, 5/7/98).

Pesticide Handlers Exposure Database

HED has used the pesticide handlers exposure database (PHED) (version 1.1) to assess handler exposure. PHED was designed by a task force of representatives from the U.S. EPA, Health Canada, the California Department of Pesticide regulation, and member companies of the American Crop Protection Association. PHED is a software system consisting of two parts - a database of measured exposure values for workers involved in the

handling of pesticides under actual field conditions, and a set of computer algorithms used to subset and statistically summarize the selected data. Currently, the database contains values for over 1,700 monitored individuals (i.e., replicates). Users select criteria to subset the PHED database to reflect the exposure scenario being evaluated. The subsetting algorithms in PHED are based on the central assumption that the magnitude of handler exposures to pesticides are primarily a function of activity (e.g., mixing/loading, applying), formulation type (e.g., wettable powders, granulars), application method (e.g., aerial, groundboom), and clothing scenarios (e.g., gloves, double layer clothing). While data from PHED provide the best available information on handler exposures, it should be noted that some aspects of the included studies (e.g., duration, acres treated, pounds of active ingredient handler) 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 can be utilized to ensure consistency in exposure assessments.

Other Assumptions for Occupational Risk Assessment

In addition to the use of standard unit exposure values based on the PHED database, the following assumptions and factors were used to complete the exposure assessment for parathion: 1) maximum label rate for each crop; 2) average body weight of an adult handler is 70 kg; 3) average work day interval represents an 8 hour workday (e.g., the acres treated or volume of spray solution prepared in a typical day); and 4) 350 acres aerial treatment per day.

9.4 Handler Risk Estimates

Table 8. Short- and intermediate-term handler risk estimates

Exposure Scenario	Restrictions / Risk Mitigation	Range of Total MOEs	
		Short-Term	Intermediate-term
1. Mixing/loading liquids for aerial applications	Baseline Clothing	0.00069 – 0.0014	0.00014 – 0.00028
2. Mixing/loading liquids for aerial applications	Maximum PPE	0.12 – 0.23	0.023 – 0.047
3. Mixing/loading liquids for aerial applications	Engineering Controls	0.23 – 0.46	0.046 – 0.092
4. Applying sprays with fjxed wing aircraft		0.39 – 0.79	0.079 – 0.16
5. Applying sprays with helicopter		0.39 – 0.79	0.079 – 0.16

Scenarios 1. and 2. are shown for comparison purposes only; baseline clothing and maximum PPE are not allowed under the 1991 Agreement. Total MOE range is determined by

specific crops; the lower MOEs represent cotton, sorghum, and sunflower and the higher MOEs represent alfalfa and canola.

9.5 Postapplication Exposure

One exposure scenario, scouting, has been selected to represent any postapplication exposure to agricultural workers. Exposure estimates for scouting are based on transfer coefficients (TC) for possible total dermal contact, estimates of available residue on plant surfaces (dislodgeable foliar residue), and the rate that ethyl parathion will decline in the environment (dissipation). The transfer coefficient for scouting is estimated to be 1,000 cm^2/hr in early season cotton and 4,000 cm^2/hr in late season cotton. It is assumed that 20 percent of ethyl parathion is available as a dislodgeable foliar residue (DFR), and that ethyl parathion dissipates at a rate of 10%per day.

Because there are cases of early entry (scouting, irrigating) into restricted-entry areas wearing PPE, an additional analysis was conducted. Assuming the addition of PPE would result in a 90 percent protection factor, transfer coefficients were adjusted to 10 percent of the standard values used above. The analysis was then conducted using transfer coefficients of 100 cm^2/hr for low crops and 400 cm^2/hr for high crops.

9.6 Postapplication Risk

The following table provides results (i.e., day after treatment where MOE is greater than 100) for an occupational surrogate Restricted-Entry Interval (REI) calculation for scouting using standard values (1 hour in treated area, TC = 1000 cm^2/hr; intermediate-term NOAEL = 0.002 mg/kg/day). All of the calculated values are significantly longer than the label REIs of 3 days. The table also provides results (i.e., day after treatment where MOE is greater than 100) for an occupational surrogate Restricted-Entry Interval (REI) calculation for scouting using PPE adjusted values (1 hour in treated area, TC = 100 cm^2/hr; Intermediate-term NOAEL = 0.002 mg/kg/day).

Table 9 Restricted-Entry Interval (REI) for each crop

Crop	Application Rate	REIs (Day when MOE is greater than 100)			
		TC =4000	TC = 1000	TC = 400	TC = 100
Alfalfa, Canola, Wheat	0.5 lb ai / acre	77	64	55	42
Barley, Corn, Soybeans	0.75 lb ai / acre	81	68	59	46
Cotton, Sorghum, Sunflower	1.0 lb ai / acre	84	70	62	49

As a verification of these standard values, a 1987 study (Ethyl Parathion: Proposal for

Reentry Interval for Cotton) that was used to set reentry intervals was re-examined. This study reports a dislodgeable foliar residue (DFR) value for the combined parathion and paraoxon residues at or below 0.06 µg per cm^2 at 72 hours (3 days) post treatment. Using this value and the current intermediate dermal endpoint, the calculated MOEs are 2 for scouting early season cotton (TC = 1000) and 1 for late season cotton (TC = 4000) assuming that the scout (without PPE) spends 1 hour per day in the treated area. Assuming that the scout wears PPE which reduces the transfer coefficients by 90 percent (TC = 100 and 400 respectively), the calculated MOEs are 23 for scouting early season cotton and 6 for late season cotton.

Although the 1991 Agreement significantly reduced occupational risk associated with parathion, the above MOE estimates for handlers of less than 1, and estimated postapplication reentry intervals greater than 40 days, demonstrate that parathion use remains a concern at this time.