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UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

WASHINGTON, D.C. 20460

OFFICE OF
PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

January 8, 1999

MEMORANDUM

SUBJECT: **CHLORETHOXYFOS**. Revised Short Format HED Chapter of RED.
Chemical Number 129006. DP Barcode D 252055.

FROM: Steven A. Knizner, Branch Senior Scientist
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TO: Deanna Scher, Chemical Review Manager
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Attached please find an updated preliminary risk assessment for chlorethoxyfos, which serves as the revised short (streamlined) format of the HED RED chapter for Chlorethoxyfos. This document contains revisions made in response to comments received during the 30-day error correction period for this preliminary HED RED Chapter.

Cumulative risk assessment considering risk from other pesticides which have a common mechanism of toxicity is not addressed in this document.

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REVISED PRELIMINARY RISK ASSESSMENT

CHLORETHOXYFOS

January 8, 199[illegible]

Health Effects Division
Office of Pesticide Programs
U.S. Environmental Protection Agency

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Executive Summary

A revised preliminary risk assessment for the chlorethoxyfos reregistration eligibility decision (RED) is presented. Based on this preliminary assessment, acute and chronic dietary (food only) risk estimates do not exceed HED's level of concern. Tier 2 (PRZM-EXAMS) surface water and ground water (SCI-GROW) estimated environmental concentrations (EECs) do not exceed HED drinking water levels of comparison (DWLOC) for both acute and chronic aggregate dietary exposure. Thus, aggregate acute and aggregate chronic risk estimates do not exceed HED's level of concern. Occupational risk estimates do not exceed HED's level of concern. Currently, there are no registered uses for chlorethoxyfos that could result in residential exposures.

Chlorethoxyfos (O,O-diethyl-O-(1,2,2,2-tetrachloroethyl)phosphorothioate) is an organophosphate insecticide registered for the control of corn rootworms, wireworms, cutworms, seed corn maggot, white grubs and symphylans on corn. Chlorethoxyfos has no other registered uses (i.e., there are no registered uses that could result in residential exposures).

E.I du Pont Nemours and Company, Inc, has registrations for the active ingredient chlorethoxyfos technical 86% (352-553) and the formulated granular products Fortress® 5G (352-552) and Fortress® 2.5G (352-579). Applications are made with ground equipment in a band over the row or in the furrow at planting. Use is limited to only one application per year, at a maximal rate of 0.1625 lb ai/A. Fortress® 5G will only be available in a SmartBox ™, which is a completely enclosed, tamper-proof delivery system.

The toxicology data base provides overwhelming evidence confirming that chlorethoxyfos, like other organophosphates, has anticholinesterase activity in all species tested, including dogs, rabbits, rats, mice, and hens. When the toxicological database for chlorethoxyfos is examined in its entirety, it can be seen that chlorethoxyfos is a potent, highly toxic organophosphate with a steep dose response curve. Females generally appear to be more sensitive than males. In some animal studies, treatment-related death was observed without accompanying clinical signs or without obvious outward signs of organophosphate toxicity.

Chlorethoxyfos technical is placed in Toxicity Category I for acute oral, dermal, inhalation, and primary eye and dermal irritation potential. Mortality was observed both in the primary eye irritation and primary skin irritation studies at low doses. In an acute neurotoxicity study, a single oral administration to rats resulted in clinical signs in both sexes and inhibition of plasma (males) and red blood cell (males and females) cholinesterase activity but no neuropathology. There was no evidence of organophosphate induced delayed neurotoxicity (OPIDN) in hens given single oral doses of chlorethoxyfos.

The requirement for a subchronic neurotoxicity study in rats was waived since several other toxicity studies in the database provided adequate evidence for the absence of neuropathology. In subchronic and chronic studies conducted with mice, rats and dogs, systemic toxicity was manifested as mortality, cholinergic signs (tremors), inhibition of plasma, red blood cell and/or brain cholinesterase activity and decreases in body weight and/or body weight gains.

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In a six month feeding study in dogs conducted to assess the ocular toxicity potential of chlorethoxyfos, no treatment-related abnormalities were found by histopathology or in most of the techniques used to assess visual system structure and function.

Chlorethoxyfos was non-mutagenic both *in vivo* and *in vitro*. Chlorethoxyfos is classified as a Group D chemical; not classifiable as to human carcinogenicity based on the lack of evidence of carcinogenic potential in mice and rats. There was no evidence of increased susceptibility following *in utero* exposures to rats and rabbits. Also, following pre/post natal exposure to rats there was no evidence of abnormalities in the development of the fetal nervous system in these studies.

The inhibition of plasma cholinesterase activity was the toxicity endpoint selected for acute and chronic dietary (oral) as well as short- and intermediate-term (dermal and inhalation) risk assessments. An Uncertainty Factor (UF) of 100 was applied to the dose selected for risk assessment to account for inter-species variation (10x) and intra-species extrapolation (10x). The additional 10x factor for the protection of infants and children as required by the Food Quality Protection Act (FQPA) of 1996 was removed based on the: 1) completeness of the toxicology database; 2) lack of increased susceptibility in developmental and reproductive toxicity studies; 3) use of adequate data (actual, surrogate, and/or modeling outputs) to satisfactorily assess dietary exposure as well as screening level drinking water exposure assessment; and 4) there are no uses that could result in residential exposures.

Five exposure and risk assessments were conducted for chlorethoxyfos for the following exposure routes and durations: acute dietary, chronic dietary, occupational short- and intermediate-term dermal, and occupational inhalation (for any time period). The acute and chronic dietary assessments capture exposure estimates for the general public. The latter of these three assessments are for occupational exposures. The five different assessments were conducted separately based on different hazards identified as toxicological endpoints

Acute dietary (food) risk estimates for chlorethoxyfos do not exceed HED's level of concern. For the acute dietary risk assessment, the toxic endpoint selected was the no observed effect level (NOEL) of 0.06 mg/kg/day based on plasma cholinesterase inhibition at a lowest observed effect level (LOEL) of 0.6 mg/kg/day observed on day 3 of a six month ocular toxicity in dogs study (feeding study). An uncertainty factor of 100 was applied to the NOEL to calculate the acute RfD. For the US population, 1% of the acute RfD was occupied and for the most highly exposed population subgroup, infants less than one year old, 3% of the acute RfD was occupied. The acute dietary exposure analysis was conducted for chlorethoxyfos using the established tolerances and assuming 100% crop treated. HED notes that no detectable residues of chlorethoxyfos were found in any of the corn residue field trials. Thus, this analysis represents a worst case estimate (Tier 1). Use of anticipated residues, Monte-Carlo analysis, and/or percent crop treated information would result in a lower dietary exposure estimate.

Chronic dietary (food) risk estimates for chlorethoxyfos do not exceed HED's level of concern. For the chronic dietary risk assessment, the toxic endpoint selected was the no observed effect level (NOEL) of 0.06 mg/kg/day based on plasma cholinesterase inhibition at a

lowest observed effect level (LOEL) of 0.6 mg/kg/day observed in the 1-year chronic feeding study in dogs, the 90-day feeding study in dogs, and the six month ocular toxicity in dogs study (feeding study). An uncertainty factor of 100 was applied to the NOEL to calculate the chronic RfD. For the US population, 1% of the chronic RfD was occupied and for the most highly exposed population subgroup, children one to six years old, 2% of the chronic RfD was occupied. The chronic dietary (food) exposure analysis was conducted for chlorethoxyfos using the established tolerances along with the assumption of 100% crop treated. HED again notes that no detectable residues of chlorethoxyfos were found in any of the corn residue field trials. Thus, this analysis for chlorethoxyfos chronic dietary exposure represents a worst case estimate (Tier 1). Use of anticipated residues, and/or percent crop treated information would result in a lower dietary exposure estimate.

The acute and chronic drinking water level of comparison (DWLOC) for the US Population is 21 ppb and for children 1-6 years old it is 6 ppb. EFED Tier 2 modeling estimates for levels of chlorethoxyfos in surface (PRZM-EXAMS) and ground water (SCI-GROW) do not exceed the DWLOC for acute or chronic aggregate exposure.

There are no registered uses for chlorethoxyfos that could result in residential exposures at the present time. Therefore, a short and intermediate-term aggregate risk assessment for the general public is not required.

Short and intermediate-term dermal and inhalation risk assessments were conducted for occupationally exposed individuals. The short- and intermediate-term dermal toxicity endpoint is the NOEL of 1.25 mg/kg/day obtained from a 21-day dermal toxicity study in rats, with an LOEL of 3.75 mg/kg/day based on erythrocyte cholinesterase inhibition. The inhalation endpoint is based on the same study as the acute dietary endpoint. HED worker exposure estimates are based on chemical specific studies which monitored the chlorethoxyfos exposure of applicators who were operating enclosed-cab tractors while applying chlorethoxyfos at the maximum label rate per acre of corn. The combined loader and applicator total dermal and inhalation risk estimates for both products do not exceed HED's level of concern.

Minimal post-application exposure is anticipated during activities such as scouting or harvesting, as chlorethoxyfos is incorporated into the soil, is not water soluble, degrades readily, is not systemic in the plant, and harvesting of corn is primarily mechanical in nature.

I. Hazard Assessment

A. Toxicology Assessment

The toxicology database for chlorethoxyfos is complete. Attachments 1-4 presents the reports of the various HED committees. The toxicology profile is presented in Table 1. Chlorethoxyfos is acutely toxic via the oral, dermal and inhalation routes of exposure, is too toxic to test for eye and skin irritation, and is not a dermal sensitizer. It did not induce OPIDN in hens nor neuropathology in rats following a single oral doses. The principal toxicological

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effects in mice, rats, and dogs following subchronic and chronic oral (dietary) exposure was inhibition of plasma, red blood cell and/or brain cholinesterase activity. In a study that examined the ocular toxicity potential, there was no treatment-related histopathology or abnormalities in most of the techniques used to assess visual system structure and function. Repeated dermal applications for 21-days resulted in inhibition of plasma, erythrocyte and brain cholinesterase activity. There was no evidence of carcinogenicity in mice and rats when tested at doses that were judged to be adequate to assess carcinogenicity. Chlorethoxyfos was non mutagenic both *in vivo* and *in vitro*. Chlorethoxyfos is classified as a Group D chemical; not classifiable as to human carcinogenicity based on the lack of carcinogenic potential which is supported by the lack of mutagenic activity. There was no evidence of increased susceptibility of rat or rabbit fetuses following *in utero* exposure in prenatal developmental toxicity studies, no offspring toxicity was seen at the highest dose tested in the two-generation reproduction toxicity study, and there was no evidence of abnormalities in the development of the fetal nervous system in these studies.

Table 1. Toxicity Profile of Chlorethoxyfos

Study Type	MRID No.	Results	Toxicity Category
Acute Oral	40883711	LD_{50} = 4.8 mg/kg (Males) 1.8 mg/kg (Females)	I
Acute Dermal	40883715	LD_{50} = 18.5 mg/kg (Males) 12.5 mg/kg (Females)	I
Acute Inhalation	40883716	LC_{50} =>0.008 mg/L	I
Primary Eye Irritation	40883717	0.1 mL too toxic; 0.05 mL caused deaths within 4 hrs.	I
Primary Skin Irritation	40883718	0.5 mL too toxic to test	I
Dermal Sensitization	40883719	Non-sensitizing	NA
Acute Delayed Neurotoxicity	40898702	Negative for OPIDN	NA
Acute Neurotoxicity	44234601	LOEL = 0.75 mg/kg/day (M) LOEL = 0.25 mg/kg/day (F) No neuropathology	NA

Study Type	MRID No.	Results
21-Day Dermal Toxicity-Rat	44399801	NOEL (ChE Inhibition) = 1.25 mg/kg/day LOEL (ChE Inhibition) = 3.75 mg/kg/day
Subchronic-Feeding-Mouse	41290629	NOEL (systemic) = 8.89 mg/kg/day LOEL (systemic) = >8.89 mg/kg/day (HDT) NOEL (ChE Inhibition)= Not established. LOEL (ChE Inhibition)= 2.19 mg/kg/day (LDT)

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Study Type	MRID No.	Results
Subchronic-Feeding-Rat	41290627	NOEL (systemic) = 0.357 mg/kg/day LOEL (systemic) = 0.784 mg/kg/day NOEL (ChE Inhibition)=0.093 mg/kg/day LOEL (ChE Inhibition)= 0.472 mg/kg/day
Subchronic-Feeding-Rat	42559215	NOEL (systemic) = 0.635 mg/kg/day LOEL (systemic) = 1.23 mg/kg/day NOEL (ChE Inhibition)=0.080 mg/kg/day LOEL (ChE Inhibition)= 0.635 mg/kg/day
Subchronic-Feeding-Dog	40898703 40898704	NOEL (systemic) = 0.185 mg/kg/day LOEL (systemic) = 1.820 mg/kg/day NOEL (ChE Inhibition)=0.017 mg/kg/day LOEL (ChE Inhibition)= 0.185 mg/kg/day
Six Month-Feeding-Dog	42559221	NOEL (systemic) = 0.061 mg/kg/day LOEL (systemic) = 0.578 mg/kg/day NOEL (ChE Inhibition) = Not established LOEL (ChE Inhibition) = 0.061 mg/kg/day
Chronic-Feeding-Dog	41736833	NOEL (systemic) = 0.616 mg/kg/day LOEL (systemic) = 2.24 mg/kg/day NOEL (ChE Inhibition)=0.063 mg/kg/day LOEL (ChE Inhibition)= 0.616 mg/kg/day
Chronic toxicity/Carcinogenicity-Rat	41736837	NOEL (systemic) = 0.311 mg/kg/day LOEL (systemic) = >0.311 mg/kg/day (HDT) NOEL (ChE Inhibition)=0.154 mg/kg/day LOEL (ChE Inhibition)= 0.311 mg/kg/day **No evidence of carcinogenicity**
Carcinogenicity-Mouse		NOEL (systemic) = 3.25 mg/kg/day LOEL (systemic) = 14.9 mg/kg/day **No evidence of carcinogenicity**
Developmental Toxicity-Rat	40898705	Maternal NOEL = 0.25 mg/kg/day LOEL = 0.50 mg/kg/day Developmental NOEL= 0.25 mg/kg/day LOEL = 0.50 mg/kg/day
Developmental Toxicity-Rabbit	41290633 42559219	Maternal NOEL = 0.76 mg/kg/day LOEL = 1.38 mg/kg/day Developmental NOEL= 1.38 mg/kg/day LOEL = 2.1 mg/kg/day
Reproductive Toxicity	41736836	Parental/Systemic NOEL = 0.296 mg/kg/day LOEL = 0.607 mg/kg/day Offspring NOEL= 0.607 mg/kg/day (HDT) LOEL >0.607 mg/kg/day (HDT)
Gene Mutation - *Salmonella*	40883726	Non-mutagenic (±)activation.

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Study Type	MRID No.	Results
Gene Mutation - HGPRT	40883727	Non-mutagenic (±)activation.
Mouse Lymphoma	40883728	Non-mutagenic (±)activation.
Micronucleus Assay	40883729	Non-mutagenic (±)activation.
DNA Repair Assay	40883730	Non-mutagenic (±)activation.
CHO Assay	40883731	Non-mutagenic (±)activation.
Metabolism-Rat	42559220 41290635	Greater than 95% of the administered radioactivity was recovered by 7 days post-dosing. Radioactivity eliminated in the urine (60-66%), feces (13-26%), expired air (11%) and tissues/ carcass (5-6%). Trichloroacetic acid, dichloroacetic acid, trichloroethanol and trichloroethanol's glucuronide conjugates (the major urinary metabolite) detected in the urine and feces. Unchanged parent was the major fecal metabolite in females, but was not detected in males.

B. Dose Response Assessment

1. Determination of Susceptibility

The Hazard Identification Assessment Review Committee (HIARC) evaluated the toxicology data base and concluded that: 1) the toxicology data base is complete; 2) neurotoxicity studies did not show evidence of OPIDN in hens, neuropathology was not seen either in the acute neurotoxicity study with rats or in the other toxicity studies, and there was no evidence of abnormalities in the development of the fetal nervous system in the pre/post natal studies; 3) there was no evidence of increased susceptibility in the prenatal developmental toxicity studies in rats and rabbits and in the two-generation reproduction study in rats; and 4) the weight-of-the evidence did not indicate the need for a developmental neurotoxicity study in rats (see Attachment 1).

The FQPA Safety Factor Committee evaluated the hazard and exposure data of chlorethoxyfos and determined that the 10x safety factor for the protection of infants and children should be removed (see Attachment 2) based on the following factors:

i. In prenatal developmental toxicity studies following *in utero* exposure in rats and rabbits, there was no evidence of developmental effects being produced in fetuses at lower doses as compared to maternal animals nor was there evidence of an increase in severity of effects at or below maternally toxic doses.

ii. In the pre/post natal two-generation reproduction study in rats, there was no evidence of enhanced susceptibility in pups when compared to adults

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(i.e., effects noted in offspring occurred at maternally toxic doses or higher).

iii. Adequate actual data, surrogate data, and/or modeling outputs are available to satisfactorily assess dietary and residential exposure and to provide a screening level drinking water exposure assessment.

2. Toxicology Endpoint Selection

The toxicology endpoints selected for dietary and non-dietary risk assessments are presented in Table 2.

Table 2. Toxicology Endpoints Selected for Risk Assessments

Exposure Duration	Exposure Route	Dose	Endpoint	Comments
Acute	Dietary	Acute RfD= 0.0006 mg/kg	Plasma cholinesterase	NOEL=0.06 mg/kg/day based on plasma ChE inhibition seen on day 3 in 6-month ocular toxicity study in dogs and an Uncertainty Factor of 100 applied. No FQPA Safety Factor.
Chronic	Dietary	Chronic RfD= 0.0006 mg/kg/day	Overall Cholinesterase inhibition (ChEI)	NOEL=0.061 mg/kg/day based on ChEI in the 90-day, 6-month and 1-year studies in dogs. An Uncertainty Factor of 100 applied. No FQPA Safety Factor.
Short-Term (1-7 Days)	Dermal	NOEL = 1.25 mg/kg/day	Erythrocyte ChEI	A MOE of 100 is adequate for occupational exposure risk assessments. **There are no residential uses.**
Intermediate-Term (7-90 days)	Dermal	NOEL = 1.25 mg/kg/day	Erythrocyte ChEI	A MOE of 100 is adequate for occupational exposure risk assessments. **There are no residential uses.**
Long-Term (several months to life-time)	Dermal	None	None	Based on the use pattern (1 application/year), there is no potential long-term dermal exposure. Therefore, this risk assessment is not required.
Short- and Intermediate-Term	Inhalation	NOEL= 0.06 mg/kg/day	Plasma cholinesterase inhibition	Oral NOEL selected due to lack of an appropriate inhalation study and the oral LD_{50} and inhalation LC_{50} for the technical and the formulation product (Fortress 5G) are both in Toxicity Category I. On this basis, the Agency has no reason to believe that chlorethoxyfos is less potent in term of toxicity by the inhalation route. Since an oral NOEL was selected, the use of 100% (default) inhalation absorption rate is required for risk assessment. A MOE of 100 is adequate for occupational exposure risk assessments. There are no residential uses.

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Exposure Duration	Exposure Route	Dose	Endpoint	Comments
Long-Term (several months to life-time)	Inhalation	None	None	Based on the use pattern (1 application/year), there is no potential long-term dermal exposure. Therefore, this risk assessment is not required.

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II. Exposure Assessment

A. Registered Uses

Chlorethoxyfos is registered for the control of corn rootworms, wireworms, cutworms, seed corn maggot, white grubs and symphylans on corn. Chlorethoxyfos is sold in the US by E.I du Pont Nemours and Company under the trade names Fortress® 5G (352-552) and Fortress® 2.5G (352-579). Fortress® is a granular soil insecticide for use on field corn, sweet corn, popcorn and corn grown for seed. The maximal amount of chlorethoxyfos applied per acre is 0.1625 lb ai/A. Applications are to be made with ground equipment in a T-band or in the furrow at planting. Fortress® is restricted to one application per year. Fortress® 5G will only be available in a SmartBox ™, which is a completely enclosed, tamper-proof delivery system.

B. Dietary Exposure

Tolerances are established (40 CFR §180.486) for residues of chlorethoxyfos in corn commodities as follows:

field corn grain	0.01 ppm
field corn forage	0.01 ppm
field corn fodder	0.01 ppm
popcorn grain	0.01 ppm
popcorn fodder	0.01 ppm
sweet corn (K + CWHR)	0.01 ppm
sweet corn forage	0.01 ppm

The nature of residue in corn and animals is adequately understood (Attachment 5, J. Stokes memo of 4/11/95). The HED Metabolism Assessment Review Committee has concluded that the residues of concern is the parent compound, chlorethoxyfos. In the corn metabolism study, no residues of the parent were found in corn commodities even after treatment at a 10x rate (MRID 41290601).

Tolerances are not required at this time for residues in milk and livestock tissues. The metabolism of chlorethoxyfos in the goat was extensive. No significant residues of parent or its oxygen analog were found. All metabolites detected were the result of re-incorporation of radioactivity in to natural products (MRID 41290602 and 41736804).

Adequate field trial data were submitted to support the established tolerances (MRID 41736815 and 417368-18). Field trials also showed no residues (<0.01 ppm) of parent in any of the corn raw agricultural commodities analyzed. On the basis of the results from both wet and dry corn processing studies (MRID 41290616 and 41736819), HED concludes that no food/feed additive tolerances are required. Based upon non-detectable chlorethoxyfos residues measured in field corn, popcorn, and sweet corn commodities (<0.01 ppm) and the results of the goat metabolism study, finite transfer of chlorethoxyfos residues is not expected to meat, fat, meat byproducts, milk, or eggs. No tolerances for meat, fat, meat byproducts, milk, or eggs are necessary. There are no CODEX, Canadian, or Mexican limits established for chlorethoxyfos. Therefore, no compatibility problem exists.

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Adequate methodology is available for analysis and enforcement of chlorethoxyfos residues (MRID 41290603). Chlorethoxyfos has been tested through the FDA Multiresidue protocols A - E. Chlorethoxyfos residues are recovered by Protocols C, D, and E, but not by Protocols A and B.

1. Acute Dietary (Food) Exposure

An acute dietary exposure analysis was conducted for chlorethoxyfos using the established tolerances. Results are summarized in Table 3. For the exposure analysis, 100% crop treated was assumed. Thus, this analysis for chlorethoxyfos acute dietary exposure represents a worst case estimate (Tier 1). Use of anticipated residues, Monte-Carlo analysis, and/or percent crop treated information would result in a lower dietary exposure estimate.

The acute dietary exposure analysis, conducted using the DRES software (B. Steinwand, 6/29/95), estimates the distribution of single-day exposures for the overall U.S. population and certain subgroups. The analysis evaluates individual food consumption as reported by respondents in the USDA 1977-78 Nationwide Food Consumption Survey (NFCS) and accumulates exposure to the chemical for each commodity. Each analysis assumes uniform distribution of chlorethoxyfos in the commodity supply.

Table 3. Acute Dietary (Food) Exposure Estimate and Percent of Acute RfD Occupied (Tier 1 Exposure Analysis).

Population Subgroup	Acute Dietary (Food) Exposure (mg/kg/day)	Percent of Acute RfD
US Population	0.000008	1%
Infants <1 year old	0.000016	3%
Children 1-6 years old	0.000012	2%

2. Chronic Dietary (Food) Exposure

A chronic dietary exposure analysis was conducted for chlorethoxyfos using the established tolerances along with the assumption of 100% crop treated. Thus, this analysis for chlorethoxyfos chronic dietary exposure represents a worst case estimate (Tier 1). Results are summarized in Table 4. Use of anticipated residues, and/or percent crop treated information would result in a lower dietary exposure estimate.

The chronic dietary exposure analysis, was also conducted using the DRES software (B.Steinwand, 5/1/95). This analysis is also based on data obtained from respondents in the USDA 1977-78 Nationwide Food Consumption Survey (NFCS).

Table 4. Chronic Dietary (Food) Exposure Estimate and Percent of Chronic RfD Occupied (Tier 1 Exposure Analysis).

Population Subgroup	Chronic Dietary (Food) Exposure (mg/kg/day)	Percent of Chronic RfD
US Population	0.000006	1%
Non-Nursing Infants <1 year old	0.000014	2%
Children 1-6 years old	0.000015	2%

C. Drinking Water Exposure

1. Acute and Chronic DWLOC

The acute and chronic DWLOC for the US Population is 21 ppb and for children 1-6 years old it is 6 ppb.

Based on the acute and chronic dietary exposure estimates presented in Tables 3 and 4, drinking water levels of comparison (DWLOCs) were calculated using the formulas presented below. A human health DWLOC is the concentration of a pesticide in drinking water which would result in unacceptable aggregate risk, after having already factored in all food exposures and other non-occupational exposures for which OPP has reliable data.

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

where acute water exposure (mg/kg/day) = aRfD - acute food exposure (mg/kg/day)

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

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

The Agency's default body weights and consumption values used to calculate DWLOCs are as follows: 70 kg/2L (adult male) and 10 kg/1L (child).

1. Surface Water

EFED (see attached memorandum from R. Matzner, 11/23/98) provided estimated environmental concentrations (EECs) for chlorethoxyfos in surface water. Based on PRZM-EXAMS modeling, the following EECs for surface water were calculated:

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Table 6. PRZM-EXAMS (Tier 2) modeling results for chlorethoxyfos in surface water.

Application Method	Acute (High) Concentration (ppb)	Chronic (60-day) Concentration (ppb)
In-Furrow	0.006	0.012
T-Band	0.427	0.080

2. Ground Water

EFED (R. Matzner, 11/23/98) provided estimated environmental concentrations (EECs) for chlorethoxyfos in ground water. Based on SCI-GROW modeling the groundwater concentration of chlorethoxyfos was estimated to be 0.002 ppb.

D. Occupational Exposure

Chlorethoxyfos can be applied with ground equipment in a T-band or in the furrow at planting. Fortress® is restricted to one application per year. DuPont has registered two products which present potential exposure for loaders, applicators, and other handlers during normal use-patterns associated with chlorethoxyfos: Fortress® 2.5G granules in 50 lb bags and Fortress® 5G SmartBox™.

Fortress® 2.5G granules are supplied in 50 lb bags, which are opened and loaded manually into hoppers mounted on mechanical planters. Due to the high vapor pressure of chlorethoxyfos, loaders acquire most of their exposure during the process of opening the bags. Hence the requirement for organic vapor/pesticide respirators. The amount of Fortress® 2.5G granules applied per acre varies from 5 to 6.5 lbs product per acre depending on row spacing.

Fortress® 5G SmartBox™ is a completely enclosed, tamper-resistant delivery system. This system is designed to significantly reduce worker exposure to this pesticide. Although in field studies worker exposures were dramatically reduced compared to mixing and applying loose granules, some problems were reported with the equipment. Such problems should be monitored by the Registrant establishing a registry of incident reports. The amount of Fortress® 5G SmartBox™ applied per acre varies from 2.5 to 3.25 lbs product based on row spacing.

Loader exposure estimates from Fortress® 5G in the SmartBox™ are based on wearing long-sleeved shirt, long pants, shoes plus socks and waterproof gloves. Loaders of Fortress® 2.5G must wear this level of protection, plus an organic vapor with pesticide prefilter or pesticide canister respirator. Applicator risk is based on the use of enclosed cab tractors. The label also requires protective eyewear for both loaders and applicators. The label should also state that contaminated eyes should be flushed for a minimum of 15 minutes. The post-application reentry interval (REI) for Fortress® is 48 hours, or 72 hours if annual rainfall is less than 25 inches. Coveralls, shoes plus socks, and waterproof gloves are required for early reentry into the treated area.

A summary of exposure estimates and risk assessments for occupational handlers is

included as Tables 7 and 8.

HED's worker exposure estimates are based on chemical specific studies which monitored the chlorethoxyfos exposure of applicators who were operating enclosed-cab tractors while applying Fortress® 5G at the maximum label rate per acre of corn. The combined loader and applicator total dermal and inhalation risks for both products do not exceed HED's level of concern (MOE_{total} = 120 for Fortress® 2.5G granular and MOE_{total} = 1200 for Fortress® 5G in the SmartBox™) when compared to the required MOE of 100.

Minimal post-application exposure is anticipated during activities such as scouting or harvesting, as chlorethoxyfos is incorporated into the soil, is not water soluble, degrades readily, is not systemic in the plant, and harvesting of corn is primarily mechanical in nature.

Table 7. Occupational Handler Exposure Estimate and Risk Assessment Summary
Chlorethoxyfos [DuPont Fortress 5G SmartBox]

		DERMAL			INHALATION			Combined MOE
		(With minimum PPE)[a]			(With no respirator)			With PPE
Application Scenario	(lb ai/day)	UE[b] mg/lb a.i.	ADD[c] (mg/kg/day)	MOE[d] NOAEL = 1.25 mg/kg	UE[e] mg x 10^{-6} ai/liter air	ADD[f] (mg x 10^{-6}/kg/day)	MOE[d] NOAEL= .06 mg/kg	MOE Total[g]
SmartBox™ using a closed-cab tractor and planter [loader]	29.25	0.0002	0.000084	15,000	0.22	1.4	43,000	11,000
[applicator]	29.25	0.00081	0.00034	3,700	0.14	27	2200	1400
[combined]	29.25	0.0010	0.00042	3,000	NA	28	2100	1200

[a] The minimum PPE for loaders is coveralls over long sleeve shirt and long pants, shoes, socks, eye protection, and waterproof gloves.
The minimum PPE for applicators in the cab is long sleeve shirt, long pants, and shoes with socks.
The minimum PPE for applicators outside the cab is coveralls over long sleeve shirt and long pants, shoes with socks, waterproof gloves and protective eyewear.

[b] UE = Dermal Unit Exposure is the amount of exposure measured in terms of mg a.i./lb a.i handled

[c] ADD(mg/kg/day) [dermal]: = unit exposure (UE) from studies in mg/lb a.i. handled * 29.25 lb a.i./day / 70 kg wt;

[d] MOE = NOAEL/ADD

[e] UE = Unit Exposure for inhalation is based upon air sampling data and is expressed in terms of nanograms (mg x 10-6) of ai per liter of air respired.

[f] ADD(mg/kg/day) [inhalation] = The UE factor is multiplied by the respiratory rate of 29 liters/minute. Loader exposure was 0.25 hours/day; applicator 7.75 hours. The total dose is divided by avg body weight for ADD: [(ng/liter * liter/min* minutes) / 70kg]

[g] MOE Total is based upon the following formula: the inverse of the sum of the inverses of the dermal and inhalation MOEs:

$$1 / (1/MOE_{dermal} + 1/MOE_{inhalation})$$; these MOE have a common endpoint

These estimates are based on data from a study which used 3.25 lb. product/acre (equivalent to 0.1625 lb a.i./acre)

Table 8. Occupational Handler Exposure Estimate and Risk Assessment Summary Chlorethoxyfos [DuPont Fortress 2.5G Granules]								
		DERMAL			INHALATION			Combined MOE
		(With minimum PPE)[a]			(With respirator for loader)			With PPE
Application Scenario	(lb ai/day)	UE[b] mg/lb a.i.	ADD[c] (mg/kg/day)	MOE[d] NOAEL= 1.25 mg/kg	UE[e] mg x 10^{-6} ai/liter air	ADD[f] (mg/kg/day)	MOE[d] NOAEL= .06 mg/kg	MOE Total[g]
Fortress 2.5G™ using a closed-cab tractor and planter [loader]	29.25	0.0024	0.0010	1300	37.5 wearing OV respirator	2.8 E-4	210	180
[applicator]	29.25	0.0023	0.00096	1300	0.7	1.3 E-4	450	330
[combined]	29.25	0.0047	0.00196	640	NA	4.1 E-4	150	120

[a] The minimum PPE for loaders is organic vapor respirator, coveralls over long sleeve shirt, long pants, shoes, socks, eye protection, and waterproof gloves
The minimum PPE for applicators in the cab is long sleeve shirt, long pants, and shoes with socks.
The minimum PPE for applicators outside the cab is coveralls over long sleeve shirt and long pants, shoes with socks, waterproof gloves and protective eyewear.

[b] UE = Unit Exposure is the amount of exposure measured in terms of mg a.i./lb a.i handled

[c] ADD(mg/kg/day): = unit exposure (UE) from studies in mg/lb a.i. handled * 29.25 lb a.i./day / 70 kg wt;

[d] MOE = NOAEL/ADD

[e] UE = Unit Exposure for inhalation is based upon air sampling data and is expressed in terms of nanograms (mg x 10-6) of ai per liter of air respired.

[f] ADD(mg/kg/day) [inhalation] = The UE factor is multiplied by the respiratory rate of 29 liters/minute. Loader exposure was 0.3 hours/day; applicator 7.7 hours. The total dose is divided by avg body weight for ADD: [(nanogram/liter * liter/min * minutes) / 70kg]

[g] MOE Total is based upon the following formula: the inverse of the sum of the inverses of the dermal and inhalation MOEs:

$1 / (1/MOE_{dermal} + 1/MOE_{inhalation})$; these MOE have a common endpoint

The study data this is based on used 6.5 lb. product/acre (equivalent to 0.1625 lb a.i./acre)

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E. Residential Exposure

There are no registered uses that would result in residential exposures at the present time.

III. Aggregate Risk Estimates and Risk Characterization

For acute and chronic dietary risk assessments, an Uncertainty Factor (UF) of 100 was applied to account for inter-species extrapolation and intra-species variability. The additional 10x factor for the protection of infants and children (as required by FQPA) was removed. The acute and chronic reference doses (acute RfD and chronic RfD) were derived by dividing the NOEL by the UF of 100.

A. Aggregate Acute Risk Estimate

The acute dietary (food) risk estimates for chlorethoxyfos do not exceed HED's level of concern. Tier 2 (PRZM-EXAMS) surface water and ground water (SCI-GROW) estimated environmental concentrations (EECs) do not exceed HED drinking water levels of comparison (DWLOC) for acute aggregate dietary exposure. Thus, aggregate acute risk estimates do not exceed HED's level of concern.

The acute dietary (food) exposure analysis was conducted for chlorethoxyfos using the established tolerances. For this risk assessment tolerance level residues were assumed for all commodities having chlorethoxyfos tolerances and 100% crop treated was assumed. Thus, this analysis for chlorethoxyfos acute dietary exposure represents a worst case estimate (Tier 1). Use of anticipated residues, Monte-Carlo analysis, and/or percent crop treated information would result in a lower dietary exposure estimate.

B. Short and Intermediate-Term Aggregate Risk Estimate

Because chlorethoxyfos does not have any registered uses that could result in residential exposures, aggregate short and intermediate-term risk assessments are not required.

C. Chronic Aggregate Risk Estimate

The chronic dietary (food) risk estimates for chlorethoxyfos do not exceed HED's level of concern. Tier 2 (PRZM-EXAMS) surface water and ground water (SCI-GROW) estimated environmental concentrations (EECs) do not exceed HED drinking water levels of comparison (DWLOC) for chronic aggregate dietary exposure. Thus, aggregate chronic risk estimates do not exceed HED's level of concern.

The chronic dietary (food) risk assessment, was also based on a worst case estimate of dietary exposure with all residues at tolerance level and 100 percent of the commodities assumed treated with chlorethoxyfos. Use of anticipated residues and/or percent of crop treated data would further reduce chronic dietary (food) exposure and risk estimates.

D. Occupational Risk Estimates

HED's worker exposure estimates are based on chemical specific studies. The combined loader and applicator total dermal and inhalation risks for both products do not exceed HED's level of concern (MOE_{total} = 120 for Fortress® 2.5G granular and MOE_{total} = 1200 for Fortress® 5G in the SmartBox™) when compared to the required MOE of 100.

IV. Data Needs

There are no data gaps for chlorethoxyfos, however, HED makes the following recommendations:

1. Fortress® 5G SmartBox™ is a completely enclosed, tamper-resistant delivery system. This system is designed to significantly reduce worker exposure to this pesticide. Although in field studies worker exposures were dramatically reduced compared to mixing and applying loose granules, some problems were reported with the equipment. **Such problems should be monitored by the Registrant establishing a registry of incident reports.**

2. Product labels requires protective eyewear for both loaders and applicators. The label should also state that contaminated eyes should be flushed for a minimum of 15 minutes.