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WASHINGTON, D.C. 20460

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

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MEMORANDUM:

Subject: Risk Assessment and Reregistration Eligibility Decision (RED) Documents for Disulfoton (Revised Risk Assessment, Phase 4). Chem. No. 032501, Rereg. Case No. 0102

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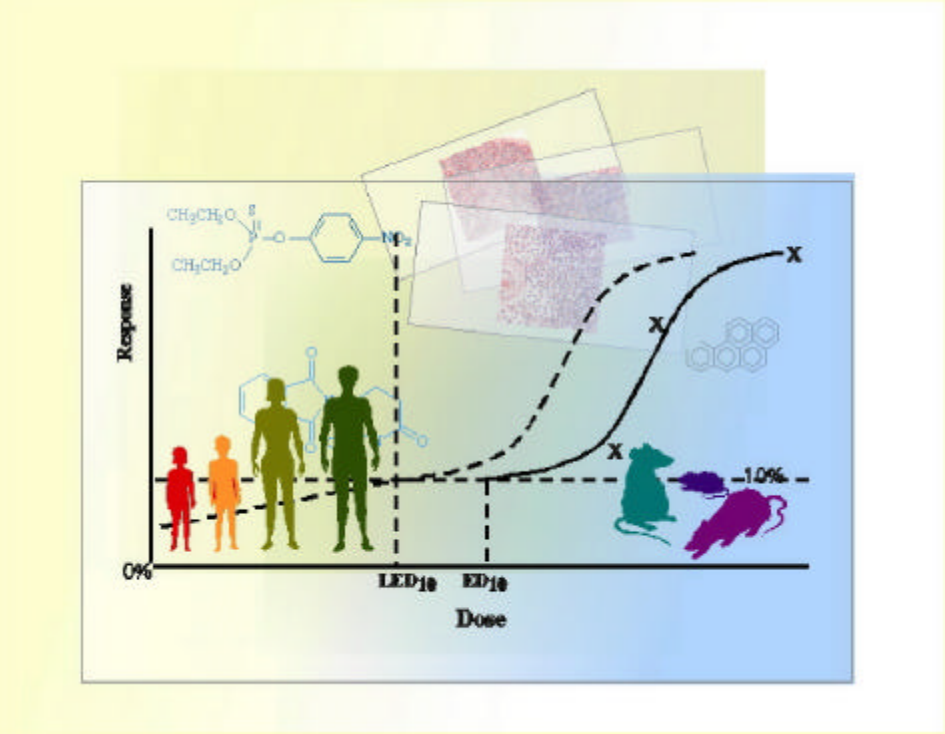
This memorandum and six appendices constitute the revised (Phase 4) Risk Assessment and Reregistration Eligibility Decision (RED) documents for disulfoton. Changes from the previous risk assessment (Phase 3) include incorporation of new data and information from revised and updated appendices. Revisions to the appendices include: major changes in the acute and chronic dietary risk to include probabilistic acute dietary risk and use of monitoring data for residues of disulfoton and metabolites of concern in food (Tier 3); minor changes in the occupational/residential exposure chapter related to public comment; inclusion of the new acute delayed neurotoxicity hen study in the toxicology chapter; the revised hazard identification assessment, and no changes in the product and residue chemistry chapter; or the incident report for disulfoton.

Consideration is also given to the Food Quality Protection Act of 1996 (FQPA). Cumulative risk assessment from other pesticides that have a common mechanism of toxicity will be addressed at a future date.

The attachments include the Revised Toxicology Chapter for the Disulfoton RED (David G Anderson, Appendix 1); the most recent Hazard Identification Assessment Review Committee (HIARC, 1/19/2000) Report for Disulfoton: Revisit (David G Anderson, Appendix 2); The FQPA Safety Factor Committee Report for Disulfoton (Brenda Tarplee, 1/24/2000, Appendix 3); the revised Disulfoton: Acute and Chronic Dietary Risk Assessment (William O. Smith, Appendix 4); the revised Product Chemistry and Residue Chemistry Chapters for Disulfoton RED (John Abbots/Ken Dockter, Appendix 5); the revised Occupational/Residential Exposure Chapter (ORE) for Disulfoton RED (Jonathan Becker, Appendix 6) and Memorandum from Jerome Blondell to Jonathan Becker of HED (3/25/1998), Review of Disulfoton Incidence Reports (Jerome Blondell, Appendix 6).

HUMAN HEALTH RISK ASSESSMENT

Disulfoton



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

David Anderson, Risk Assessor
February 10, 2000

HUMAN HEALTH RISK ASSESSMENT

Disulfoton

Phase 4

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1.0 EXECUTIVE SUMMARY[1]

Introduction

This risk assessment is being conducted on the organophosphate pesticide, disulfoton, for reregistration. Disulfoton (O,O-diethyl S-[2-(ethylthio)ethyl] phosphorodithioate) is an acaricide and insecticide currently registered by Bayer Corporation for application to grains, vegetables, cotton, and other crops.

Technical disulfoton contains 98.5 percent active ingredient (ai). Formulations include the emulsifiable concentrate (17.5 percent-85 percent ai) and the granular (0.37 percent-15 percent ai). The two percent and 15 percent granular, 95 percent ready-to-use (RTU), and the 8 lb/gal emulsifiable concentrate (EC) formulations are the disulfoton formulation classes registered for use on food/feed crops.

Applications are made with ground and aerial equipment, as well as hand-held equipment. Application rates range from 0.005 lb ai/1000 ft^2 to over 100 lb ai/A. Disulfoton is registered for use on both occupational and non-occupational use-sites including, but not limited to, food and feed crops, nut trees, non-bearing fruit trees, ornamental flowers, shrubs and trees, potted plants, residential rose bushes, and residential vegetable gardens. The registrant has agreed to discontinue disulfoton use on vegetable gardens.

Exposure to disulfoton and its cholinesterase inhibiting metabolites occurs through exposure to residues in food and water; through mixing, loading, application, and other handling procedures; and from dislogeable residues on treated plants. Residential exposure can occur through food, water, home garden use, and flower and ornamental disulfoton application and uses. The potential problem of exposure to children from hand-to-mouth exposure in treated areas was shown to be below the Agency's level of concern.

[1]In this document, risk estimates are presented as a percentage of the population adjusted dose (aPAD or cPAD) and occupational/residential risk is estimated as Margin of Exposure (MOE). Dietary exposure greater than 100 percent of the PAD is a risk of concern and MOEs less than 100 are a risk of concern for occupational/residential and aggregate exposure (water, diet and residential).

Toxicity, Dose-Response, and the FQPA Factor

Toxicity endpoints selected for risk assessment are based on cholinesterase inhibition. Disulfoton is an organophosphate, causing cholinesterase inhibition at low dose levels and across species. No neuropathy is seen in any of the studies. Brain, plasma and erythrocyte cholinesterase inhibition all occurred at the same dose level in many, but not all, studies. Females are slightly more sensitive than males.

An uncertainty factor (UF) of 100X was applied to the risk assessment to account for inter- and intraspecies variation. The FQPA safety factor (as required by the Food Quality Protection Act of August 3, 1996) was reduced to 1X because disulfoton studies show no increased susceptibility to infants and children, and no neuropathy was seen in any study.

Current reassessed tolerances are based on submitted field trial data on disulfoton, its oxygenated metabolite (demeton-S), and the corresponding sulfoxide and sulfone metabolites. In plants, disulfoton is rapidly converted to disulfoton sulfoxide and sulfone or disulfoton oxygen analog sulfoxide and sulfone (demeton-S sulfone). When the sulfur-containing side chain is removed, the products are no longer cholinesterase inhibitors. The tolerance expression for disulfoton is composed of disulfoton and its five metabolites expressed as disulfoton. This risk assessment includes all supported crops and use sites listed on the current labels.

Dietary Risk Assessment

The revised acute (probabilistic assessment) and chronic dietary exposure assessment represent the most highly refined dietary assessments possible with the data available. The revised assessments were based on data from the U.S. Department of Agriculture (USDA) Continuing Survey of Food Intake by Individuals, monitoring data from USDA Pesticide Data Program (PDP) and the Food and Drug Administration (FDA) monitoring program, field trial data, processing factors from the registrant, published literature, and percent crop treated information. The monitoring data showed few detections for disulfoton or its five metabolites, thus anticipated residues were estimated by one-half-the-limit-of-detection (½ LOD) for disulfoton and its metabolites that were likely to be present for all non-detectable residues.

The acute dietary exposure is below the Agency's level of concern (<100 percent acute Population Adjusted Dose, or aPAD[2]). The most highly exposed groups are children one to six years old and infants less than one year, both with 9.6 percent (at the 99.9th percentile) of the aPAD. The remaining groups show an acute risk that ranges from 4.7 percent to 8.8 percent of the aPAD at the 99.9th percentile exposure.

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[2]PAD = Population Adjusted Dose = $\frac{\text{Acute or Chronic RfD}}{\text{FQPA Safety Factor}}$

The chronic dietary exposure is below the Agency's level of concern (<100 percent chronic Population Adjusted Dose, or cPAD). The most highly exposed group is children one to six years old with 3.5 percent of the cPAD. The remaining groups show a chronic dietary risk that ranges from 0.87 percent to 2.4 percent of the cPAD.

Drinking Water Assessment

Most monitoring data for drinking water were inadequate; therefore, drinking water levels of comparison (DWLOCs) were calculated and compared with surface water concentration levels estimated from the Tier 2 PRZM/EXAMS model, and groundwater concentration levels estimated from the SCI-GROW model of disulfoton in water. Exposure to disulfoton through drinking water may be of concern when calculated DWLOCs are lower than the estimated environmental concentrations of disulfoton in water. PRZM/EXAMS and SCI-GROW model estimates are conservative and thus tend to over estimate concentration levels of disulfoton that may be present in ground and surface water. The limited quality assured monitoring data supported the SCI-GROW modeling values for groundwater and showed that SCI-GROW values were reasonably accurate for vulnerable areas.

Modeled surface water estimates are higher than the acute DWLOCs for the highest exposed group through food (children one to six years), which indicates that disulfoton in surface water may be an acute risk of concern. Modeled groundwater estimates are lower than the acute DWLOC for the most exposed population, which indicates that disulfoton and residues in groundwater may not be of concern. For chronic exposure, surface water and groundwater estimates are higher than the chronic DWLOCs for the highest exposed group through food (children one to six years), which indicates that disulfoton and residues in surface and groundwater may be a chronic risk of concern.

Occupational and Residential Risk Assessment

Endpoints used for occupational and residential assessments were based on cholinesterase inhibition seen in a dermal study for short-term exposure (one to seven days) and an oral study for intermediate exposure (one week to several months). A 36 percent oral equivalent dermal absorption value was used for the intermediate exposure assessment. An inhalation endpoint was based on an inhalation study for both short-term and intermediate-term exposure.

For most occupational pesticide handler scenarios exceed the Agency's level of concern. With engineering controls in place, only four of the 20 occupational scenarios showed risks that do not exceed the Agency's level of concern. Based on acute toxicity category of I, postapplication reentry intervals (REIs) are 48 hours after treatment with liquid disulfoton at 4.0 lb ai/A or lower rates of application. Reentry intervals, using standard values are estimated to be 28 to 36 days at higher rates of application of disulfoton.

Scenarios that do not exceed the Agency's level of concern for residential handler uses are limited to ornamentals and garden use at the lowest application rates. Postapplication risks for adult homeowners were estimated to be low. Toddlers, with hand-to-mouth exposures in treated areas, do not exceed the Agency's level of concern.

Aggregate and Cumulative Risk Assessment

An aggregate risk assessment (food, drinking water, and residential) was not conducted for disulfoton. All of the residential exposure scenarios specified on the label exceed the Agency's level of concern (MOEs < 100) at the maximum use rate. Estimated environmental concentrations of disulfoton residues in water are above the Agency's level of concern. Any aggregation of exposure to disulfoton through residential uses and drinking water would only serve to increase the Agency's level of concern.

The Agency is in the process of formulating guidance for conducting cumulative assessment. When this guidance is complete, the cumulative risk from all organophosphates will be assessed where appropriate.

Codex

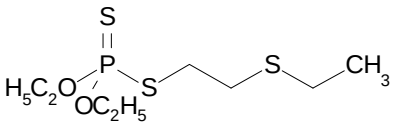
Some minor revisions in the tolerance expression are required for harmonization with Codex. Tolerances that are currently expressed as demeton-S should be expressed as disulfoton.

Conclusion

In summary, exposure to disulfoton in the diet is below the Agency's level of concern for both acute and chronic food exposure, but most occupational and residential exposures exceed the Agency's level of concern even with engineering controls (when applicable). Acute and chronic DWLOCs for surface water may be a risk of concern, and chronic DWLOC compared with the groundwater estimates may show a risk of concern.

2.0 PHYSICAL/CHEMICAL PROPERTIES CHARACTERIZATION

Disulfoton is a colorless to yellow liquid with a boiling point of 62°C at 0.01 mm Hg, vapor pressure 1.8×10^{-4} millibars at 20°C. The vapor pressure of disulfoton is moderately high, suggesting that inhalation of disulfoton may contribute to exposure under certain circumstances. Disulfoton is soluble in water at 25 ppm at 20°C and is miscible in dichloromethane , hexane, 2-propranol and toluene at 20°C. Disulfoton is an organophosphate insecticide with a molecular weight of 274.4 g/mole. The systematic name is O,O-diethyl S-[2-ethylthio)ethyl] phosphorodithioate with a trade name of Di-Syston(R). The structure is presented below.



Empirical Formula: $C_6H_{19}O_2PS_3$
Molecular Weight: 274.4 g/mole
CAS Registry No.: 298-04-4
Chemical No.: 032501

3.0 HAZARD CHARACTERIZATION

3.1 Hazard Profile

Disulfoton is acutely toxic by the oral, dermal and inhalation routes (Table 1). Disulfoton was too toxic for guideline studies on primary eye, skin irritation and dermal sensitization to be conducted. The data requirements were waived because of the severity of the anticipated results and the most severe categories should be assumed for eye and skin irritation.

The mode of action of disulfoton is inhibition of cholinesterase. In all of the toxicity studies evaluated in this hazard assessment, the LOAEL and NOAEL were established by the inhibition of cholinesterase (the basis for all regulatory endpoints). Clinical signs, such as muscle fasciculation and tremors are seen either at higher dose levels or at the LOAEL some studies. All three cholinesterases (plasma, erythrocyte and brain) are inhibited at the LOAEL in at least one study in the rat, mouse, rabbit and dog and are likely to occur across species. Slight species differences occur, but the differences may be due to normal variation and differences in the duration of the studies conducted in different species. Adult females appear to be slightly more sensitive than males. In a six-month study in rats (MRID# 43058401), cholinesterase inhibition was seen only in females at the LOAEL.

Table 1: Acute Toxicity of Disulfoton Technical				
Guideline No.	**Study Type**	**MRID #(S).**	**Results**	**Toxicity Category**
81-1	Acute Oral	Acc# 072293, Doc# 003958, p41	LD_{50} = M: 6.2 mg/kg; F:1.9 mg/kg	I
81-2	Acute Dermal	Acc# 07793, Doc# 03958, p71 & 004223, p24	LD_{50} = M: 15.9 mg/kg; F: 3.6 mg/kg	I
81-3	Acute Inhalation	Acc# 258569, Doc# 05789	LC_{50} = M: 0.06 mg/L; F: 0.015 mg/L	I
81-4	Primary Eye Irritation	Data requirement waived. Doc# 03958, p12; 004223, p14		I (assumed)
81-5	Primary Skin Irritation	Data requirement waived. Doc# 03958, p12; 004223, p14		I (assumed)
81-6	Dermal Sensitization	Data requirement waived. Doc# 03958, p12		Sensitizer (assumed)
81-7	Acute Delayed Neurotoxicity	MRID# 44996401, Doc# 013957	Negative for OPIDP	

The cholinesterase endpoints between acute and chronic studies in rats all are approximately within a 10 fold exposure level. Longer exposure always showed cholinesterase inhibition at a lower dose level. Clinical signs occurred in test animals at the same dose level as cholinesterase inhibition in the acute neurotoxicity study, whereas in the 90-day neurotoxicity study, cholinesterase inhibition occurred at a lower dose level. Motor activity was affected at lower dose levels in the 90-day study than in the acute study, but no treatment related or significant neuropathology occurred either acutely or in the 90-day studies.

No definitive endocrine disruption was seen in any of the studies. Absolute testes and ovarian weights were decreased (of unknown cause) at the highest dose level and in the presence of cholinesterase inhibition and well above the NOAEL in the chronic rat study. See Section 6.0 on Endocrine Modulation for the Agency's plans for implementation of tests on pesticides for possible endocrine affects.

There is an adequate dermal absorption study in rats and an adequate 21-day dermal study in rabbits showing cholinesterase inhibition (plasma, erythrocyte and brain).

Acceptable studies in rats and mice did not demonstrate evidence of carcinogenicity.

Disulfoton is positive in some mutagenicity studies without activation, but negative or weakly positive with activation in most. The mutagenicity database is complete for the pre-1990 required three mutagenicity categories and the *in vivo* database support a lack of concern for the mutagenicity of disulfoton.

The metabolism of disulfoton was studied in the rat. Disulfoton was found to be rapidly absorbed and excreted with over 95 percent of the administered C^{14} labeled disulfoton being recovered in the urine. Approximately 90 percent of the disulfoton was excreted within 24 hours. Less than two percent was recovered from the feces. Bioaccummulation was not observed with less than 0.3 percent being recovered in tissues and less than one percent being recovered in the carcass. A major metabolite was incompletely identified, but it co-chromatographed with 1-(ethylsulfonyl)-2-(methylsulfonyl)ethane, a fully oxidized form of the putative hydrolysis product. The toxic metabolites of disulfoton are disulfoton sulfoxide, disulfoton sulfone, disulfoton oxygen analog (demeton-S), disulfoton oxygen analog sulfoxide and disulfoton oxygen analog sulfone. The Metabolism Committee determined that the residues to be regulated in plant and animal commodities are disulfoton and these five disulfoton metabolites.

There is no increased susceptibility to fetuses or pups in acceptable developmental and reproductive toxicity studies in the rabbit or rat. In the study on reproduction, cholinesterase was inhibited (plasma, erythrocyte and brain) in parents at lower dose levels than in pups. Pup death occurred at the highest dose tested in the study on reproduction. The deaths were attributed to an inadequate milk supply and maternal care failure. In the developmental toxicity study in the rat, developmental toxicity occurred at higher doses than caused toxicity in dams. Developmental toxicity in the rat was seen in the form of incomplete ossification, but no developmental toxicity was seen in the rabbit at the adequate dose levels administered. No fetal or offspring sensitivity issues or neuropathology was identified in the toxicology database.

The toxicity profile of disulfoton is presented in Table 2. The toxicity database for disulfoton is adequate to support reregistration. The database is of generally high quality with better than average consistency in data on the dose and treatment relationship of plasma, erythrocyte and brain cholinesterase inhibition which are the regulatory endpoints of concern.

All the toxicity data used to select endpoints for regulation were acceptable guideline studies.

Table 2: Toxicity Profile of Disulfoton Technical		
Study Type	**MRID No.**	**Results**
Acute Neurotoxicity - Rat	42755801	NOAEL (Clinical signs and ChE Inhibition) = 0.25 mg/kg/day LOAEL (Clinical signs and ChE Inhibition) = 0.75 mg/kg/day
Acute Inhalation - Rat	Acc#258569	NOAEL (ChE Inhibition) = 0.0005 mg/L LOAEL (ChE Inhibition) = 0.0018 mg/L
21-Day Dermal Toxicity-Rabbit	00162338	NOAEL (Systemic) = 1.6 mg/kg/day LOAEL (Systemic) = 6.5 mg/kg/day NOAEL (ChE Inhibition) = 0.4 mg/kg/day LOAEL (ChE Inhibition) = 1.6 mg/kg/day
Subacute Inhalation - Rat (3-5 day exposures)	Acc#258569	NOAEL (ChE Inhibition) = Not established LOAEL (ChE Inhibition) = 0.0005 mg/L
Subchronic Inhalation - Rat	41224301	NOAEL = (ChE Inhibition) = 0.00016 mg/L LOAEL = (ChE Inhibition) = 0.0014 mg/L
Subchronic Neurotoxicity -Rat	42977401	NOAEL (Clinical signs) = 0.071 mg/kg/day LOAEL (Clinical signs) = 0.315 mg/kg/day (HDT) NOAEL (ChE Inhibition)= Not established. LOAEL (ChE Inhibition)= <0.071mg/kg/day (LDT)
Subchronic-Feeding-Rat		Data waived because an adequate chronic study was available
Special 6-Month Cholinesterase - Rat - Non-guideline study	43058401	NOAEL (ChE Inhibition) = 0.03 mg/kg/day LOAEL (ChE Inhibition) = 0.07 mg/kg/day
Subchronic-Feeding-Dog		Data waived because an adequate chronic dog study was available
Chronic-Feeding-Dog (1-year)	44248002	NOAEL (ChE Inhibition)=0.013 mg/kg/day LOAEL (ChE Inhibition)= 0.094 mg/kg/day
Chronic-Feeding-Dog (1-year)	00073348	NOAEL = (ChE Inhibition) = 0.25 mg/kg/day LOAEL (ChE Inhibition) = 0.05 mg/kg/day
Chronic Toxicity/Carcinogenicity-Rat	00146873 41850001 41850002	NOAEL (systemic) = 0.04 mg/kg/day LOAEL (systemic) = 0.165 mg/kg/day (HDT) NOAEL (ChE Inhibition) = Not demonstrated LOAEL (ChE Inhibition) = 0.04 mg/kg/day (LDT) **No evidence of carcinogenicity**
Carcinogenicity - Mouse	00129456 00139598	NOAEL (ChE Inhibition) = 0.6 mg/kg/day LOAEL (ChE Inhibition) = 2.4 mg/kg/day (HDT) **No evidence of carcinogenicity**
Developmental Toxicity-Rat	00129458	Maternal: NOAEL = 0.1 mg/kg/day LOAEL = 0.3 mg/kg/day Developmental: NOAEL = 0.3 mg/kg/day LOAEL = 1.0 mg/kg/day

Table 2: Toxicity Profile of Disulfoton Technical		
Study Type	**MRID No.**	**Results**
Developmental Toxicity-Rabbit	00147886	Maternal: NOAEL = 1.0 mg/kg/day LOAEL = 1.5 mg/kg/day Developmental: NOAEL= >3.0 mg/kg/day LOAEL = >3.0 mg/kg/day
Reproductive Toxicity - Rat	44440801	Parental/ Systemic: NOAEL = Not established LOAEL = 0.025 mg/kg/day (LDT) Offspring: NOAEL = 0.10 mg/kg/day LOAEL = 0.45 mg/kg/day (HDT)
Reproductive Toxicity - Rat	00157511	Parental/ Systemic: NOAEL = 0.04 mg/kg/day LOAEL = 0.12 mg/kg/day Offspring: NOAEL = 0.04 mg/kg/day LOAEL = 0.12 mg/kg/day
Gene Mutation - *Salmonella*	00028625	Non-mutagenic (±) activation.
Gene Mutation - HGPRT	40638401	Assumed + because tested at partially soluble conditions.
Chromosomal Aberrations	43615701	Non-mutagenic (±) activation.
Sister Chromatide Exchange	40495001	Non-mutagenic (-) activation, but (+) with activation.
Sister Chromatide Exchange	Acc#072293	Non-mutagenic (±) activation
Unscheduled DNA Synthesis	Acc#028625	Mutagenic (+) activation, but non-mutagenic (-) activation
Mouse Lymphoma	EPA-600/1-84-003	Mutagenic (+) activation, but non-mutagenic (+) activation.
Mouse Micronucleus	EPA-600/1-84-003	Non-mutagenic.
Sister Chromatide Exchange	EPA-600/1-84-003	Weakly mutagenic (-) activation, but non-mutagenic (+) activation

Table 2: Toxicity Profile of Disulfoton Technical		
Study Type	**MRID No.**	**Results**
Metabolism-Rat	42565101	Greater than 90 percent of the administered radioactivity was metabolized completely and eliminated within 24 hours. About 95 percent of the radiolabel was recovered in the urine, <2 percent in the feces, <0.3 percent in tissues and <1 percent in the carcas. No bioaccummulation was noted. Sex related differences were attributed to different metabolic rates rather than different profiles. The (toxicologically inactive) major and minor metabolites were produced by hydrolysis of oxygen metabolites.
Dermal Absorption - Rats	43360201	Dermal absorption is considered to be 36 percent at 10 hours

3.2 Endpoint Selection

Table 3 shows the acute and chronic dietary exposure endpoints. Table 4 shows the NOAELs, endpoints, and MOEs selected for residential and occupational exposure.

Table 3: Endpoints Selected for Acute and Chronic Dietary Exposure			
Exposure Scenario	**Study**	**NOAEL[1]**	**Endpoint**
Acute dietary	Acute neurotox/rat (81-8)	0.25 mg/kg/day	Cholinesterase inhibition and muscle fasciculation was seen in females at 0.75 mg/kg/day
	Acute dietary PAD = 0.0025 mg/kg (NOAEL/100)		
Chronic dietary	Chronic/Dog (83-1)	0.013 mg/kg/day	Plasma, erythrocyte, brain and retinal cholinesterase inhibition was seen in females at 0.094 mg/kg/day
	Chronic dietary PAD = 0.00013 mg/kg/day (NOAEL/100)		

Table 4: Endpoints Selected for Occupational and Residential Exposure Scenarios			
Exposure Scenario	**Study**	**NOAEL[1]**	**Endpoint**
Short-term (dermal)	21-day dermal/rabbit (82-3)	0.4 mg/kg/day	Plasma, erythrocyte and brain cholinesterase inhibition was seen in males and females at 1.6 mg/kg/day
	Correction for dermal absorption unnecessary (MOE necessary is 100)		
Intermediate-term (dermal)	6-month oral chronic/rat	0.03 mg/kg/day [2]	Plasma, erythrocyte and brain cholinesterase inhibition was seen in females at 0.7 mg/kg/day
	Correction for oral to dermal exposure necessary (MOE necessary is 100)		
Long- term (dermal)	Chronic oral/dog (83-1)	0.013 mg/kg/day [2]	Plasma, erythrocyte, brain and retinal cholinesterase inhibition was seen in females at 0.094 mg/kg/day
	Correction for oral to dermal exposure necessary (MOE necessary is 100)		
All Time Periods Short-Intermediate and Long-term (inhalation)	90-day inhal/rat (82-4)	0.00016 mg/L	Plasma, erythrocyte and brain cholinesterase inhibition was seen in males and females at 0.0014 mg/L
	Inhalation (MOE necessary is 100)		

[1] = No Observed Adverse Effect Level.
[2] = Appropriate route-to-route extrapolation should be performed for these risk assessments (i.e., oral to dermal components use absorption rates of 36 percent).

3.3 FQPA Considerations

The Hazard Identification Assessment Review Committee (HIARC) recommended that the FQPA safety factor be removed for disulfoton (A Combined Report of the Hazard Identification Assessment Review Committee, 1/19/2000 and the FQPA Safety Factor Committee, 1/24/2000). The toxicity database is complete including neurotoxicity studies in rats and there is no evidence of either neurotoxicity or increased susceptibility of fetuses or offspring in prenatal and postnatal studies in rabbits or rats.

The committee determined that the 1X FQPA factor is applicable for all populations.

4.0 EXPOSURE ASSESSMENT

4.1 Summary of Registered Uses

Disulfoton is an organophosphate insecticide/acaricide registered by Bayer Corporation under the trade name DiSyston®. Disulfoton is registered in the United States for preplant, at-planting, preemergence and foliar applications. Formulations include the 98.5 percent active ingredient (ai) technical product, an emulsifiable concentrate (17.5 percent to 85 percent ai), and a granular (0.37 percent to 15 percent ai).

Disulfoton has been registered for use on both occupational and non-occupational use-sites. Occupational use-sites include food and feed crops, nut trees, non-bearing fruit trees, ornamental flowers, shrubs and trees, and potted plants. Non-occupational use-sites include residential ornamental flowers, shrubs and trees, residential rose bushes, residential vegetable gardens (proposed for deletion), and residential potted plants. Application rates range widely from 0.005 lb ai/1000 ft^2 to over 100 lb ai/A. Disulfoton is applied with ground and air equipment as well as hand-held equipment.

4.2 Dietary Exposure from Food

The Metabolism Committee concluded that residue to be regulated in plants include parent disulfoton and five metabolite expressed as disulfoton (Table 5).

In plants, disulfoton is rapidly converted to disulfoton sulfoxide and sulfone or disulfoton oxygen analog sulfoxide and sulfone (demeton-S sulfone). When the sulfur-containing side chain is removed, the products are no longer cholinesterase inhibitors.

In ruminants and poultry, of the six metabolites of concern, only parent disulfoton was identified.

The analytical methods for enforcement and data collection involve oxidation of disulfoton and its metabolites to the corresponding sulfones. It should be noted the method of analysis for USDA Pesticide Data Program (PDP) and the Food and Drug Administration (FDA) data analyzes for disulfoton and each metabolite individually where analyzed because the oxidation step is not included. The PDP included some but not all metabolites.

Tolerances for disulfoton residues in food were reassessed and range from 0.01 ppm for milk to 5.0 ppm for oats and wheat folder. For additional details see Appendix 4.

Table 5: Common and Chemical Names of Identified Disulfoton Tolerance Residues	
I. Disulfoton O,O-diethyl S-[2-(ethylthio)ethyl]phosphorodithioate	**IV. Disulfoton oxygen analog; Demeton-S** O,O-diethyl S-[2-(ethylthio)-ethyl]phosphorothioate
II. Disulfoton sulfoxide O,O-diethyl S-[2-(ethylsulfinyl)ethyl]phosphorodithioate	**V. Disulfoton oxygen analog sulfoxide** O,O-diethyl S-[2-(ethylsulfinyl)-ethyl]phosphorothioate
III. Disulfoton sulfone O,O-diethyl S-[2-(ethylsulfonyl)ethyl]-phosphorodithioate	**VI. Disulfoton oxygen analog sulfone** O,O-diethyl S-[2-(ethylsulfonyl)-ethyl]phosphorothioate

4.2.1 Acute and Chronic Dietary Exposure Methodology and Characterization

The acute and chronic dietary risk assessments are performed using DEEM® software. The dietary exposure estimates are the most refined possible from the data available. For the current Tier 3 dietary risk estimates, a probabilistic model (Monte Carlo) was used for acute dietary risk and deterministic methodology utilizing average food consumption was used for chronic dietary risk.

USDA's Pesticide Data Program (PDP) and the Food and Drug Administration (FDA) data were used for detectable levels of disulfoton and metabolites of concern. PDP and FDA collect residue data on large food samples (generally 5 lb or more). The data is collected in a statistically sound manner and under Good Laboratory Practices that are approved by the Agency.

For the acute dietary assessment, all single serving food forms included in the disulfoton assessment, and for which monitoring data were used include asparagus, broccoli, cabbage, cauliflower, sweet corn, head lettuce, leaf lettuce, sweet peppers, potatoes, and tomatoes.

Combining ½ LODs for disulfoton and its five metabolites for non-detects may over estimate the probable levels of these residues. The ½ LOD procedure was modified to include ½ LOD for parent and those metabolites that were likely to occur (estimated from field trial and metabolism data which indicated only three of the five metabolites were likely to occur). This method yields conservative estimates of the possible residue levels, and will not underestimate these levels. For details on the use of this method to modify the use of ½ LOD for disulfoton and all five metabolites in estimating appropriate values for non-detectable residues, see Monitoring Data, in Appendix 4.

Percent Crop Treated Data

A quantitative usage analysis was provided by OPP's Biological and Economic Analysis Division (BEAD) based on data years 1987-98 (Steven M. Nako, QUA date: May 5, 1999). Data sources included USDA/NASS (1990-97), California EPA, Department of Pesticide Regulation (1993-96), National Center for Food and Agricultural Policy (1992), and various proprietary data sources including Doane (1987-98), Maritz, and Mike Buckley (1994-97).

Contribution of potential residues from crops with import tolerances was based on information provided by Bayer Corporation (MRIDs 44821701 & 44821702). As a default assumption, all imports from countries approved for disulfoton use on coffee, hops, and rice were included, and of these imports 100 percent were assumed treated with disulfoton. Additionally, only Argentina has a registration for disulfoton on hops but in the submitted analysis 100 percent of the imported hops and imported beer (from all countries) was considered as treated. The registrant's proposal for these crops is acceptable and, in the absence of more refined data, will be used in estimating residues on these crops.

Food Processing Factors

The registrant has included processing information in their most recent refined dietary assessments (explained and documented in MRIDs 44821701 & 44821702). These factors were based on several Bayer reports as well as published articles from the scientific literature and were used by Bayer to adjust residue values derived from field trial data. These reports have been reviewed and, where applicable, the data have been incorporated in the dietary risk assessment.

4.2.2 Acute Dietary Risk (Food)

The most highly refined acute dietary risk using available data is presented below in Table 6. The highest acute dietary risk is 9.6 percent of the aPAD at the 99.9th percentile for children one to six years old. The acute dietary risk for the general population is seven percent of the aPAD at the 99.9th percentile. See table 6 for the acute dietary risk for other subpopulations.

An extensive sensitivity analysis has not been conducted; however, it would be expected that the critical commodities would be high consumption items that have residues on them. The succulent beans have the most delectable residues from monitoring data, although they are few and at low levels. For additional details see Appendix 4.

Table 6: Acute Dietary Risk Estimates (aPAD = 0.0025 mg/kg/day)						
Population	**95th percentile**		**99th percentile**		**99.9th percentile**	
	Exposure	**% aPAD**	**Exposure**	**% aPAD**	**Exposure**	**% aPAD**
US pop-All seasons	0.000031	1.2	0.000065	2.6	0.000176	7.0
All infants (<1 yr)	0.000043	1.7	0.000074	3.0	0.000218	8.7
Children (1-6 yr)	0.000063	2.5	0.000116	4.6	0.000239	9.6
Children (7-12 yr)	0.000041	1.6	0.000076	3.0	0.000203	8.1
Females (13+/preg/not nursing)	0.000019	0.76	0.000033	1.3	0.000084	3.4
Males (20+ yr)	0.000021	0.84	0.000046	1.8	0.000148	5.9
Seniors (55+)	0.000019	0.78	0.000045	1.8	0.000184	7.4
DEEM ® (Ver 6.78), Acute analysis disulfoton based on 1989-92 data.						

4.2.3 Chronic Dietary Risk (Food)

The estimates of chronic dietary exposures from uses of disulfoton on food and feed crops are shown in Table 7. The highest chronic food exposure was to children one to six years old at 3.5 percent of the cPAD. The chronic dietary risk for the general population is 2.3 percent of the cPAD.

For chronic dietary risk the chronic module version 6.76 of DEEM™ was used and is the most highly refined possible with the data available. Human consumption of the various commodities was estimated from the 1989 - 1992 USDA *Continuing Surveys of Food Intake for Individuals*. The chronic assessment incorporated average residues of disulfoton and its five metabolites of concern from monitoring data and field trials, adjusted for percent crop treated and for residue reduction or concentration from processing and cooking. For additional details see Appendix 4.

Table 7: Chronic Dietary Risk Estimates (cPAD = 0.00013 mg/kg/day)		
Population	**Average Exposure (mg/kg/day)**	**% cPAD**
US population (total)	0.000003	2.3
All infants (<1 yr)	0.000001	0.9
Children (1-6 yr)	0.000005	3.5
Children (7-12 yr)	0.000003	2.4
Females (13-19 not preg or nursing)	0.000002	1.4
Females (20+ yr not preg or nursing)	0.000003	2.3
Females (13+ preg/not nursing)	0.000002	1.3
Females (13+ yr nursing)	0.000002	1.9
Males (20+ yr)	0.000003	2.4
Seniors (55+)	0.000003	2.5
DEEM ® (Ver. 6.76) Chronic dietary analysis for disulfoton using 1989-92 data; Adjustment factor #2 used		

4.3 Water Exposure (Drinking Water Sources)

Potential exposure to disulfoton in drinking water was assessed using modeling and limited monitoring data. The data were provided by the Environmental Fate and Effects Division (EFED)(Memorandum from Kathryn Montague, John Jordon, James Wolf, and Mary Frankenberry to Christina Scheltema, SRRD (amended 10/07/99 from 8/26/99). The major routes of dissipation are microbial degradation in an aerobic soil and aqueous photolysis and soil photolysis. Limited data suggest that the sulfoxide and sulfone degradates are much more persistent than the parent.

4.3.1 Surface Water

A Tier 2 assessment was conducted using PRZM/EXAMS modeling based on the fate profile for disulfoton, disulfoton sulfoxide, and disulfoton sulfone, as well as maximum registered application rates. The maximum peak concentration of parent disulfoton and cholinesterase inhibiting residues was estimated at 58 μg/L and the estimated maximum mean of annual averages is 9.3 μg/L.

4.3.2 Groundwater

The SCI-GROW (Screening Concentrating in Groundwater) screening model was used to estimate potential groundwater concentrations for disulfoton parent and residues. At the maximum application rate, the maximum predicted disulfoton and residue groundwater concentration was 3.2 μg/L from SCI-GROW models. Groundwater levels from SCI-GROW are supported by the 2.9 μg/L from limited monitoring data (see Section 4.4.3).

4.3.3 Monitoring Data

Surface water monitoring data collected by the USGS as part of the National Water Quality Assessment (NAWQA) program was also considered. Disulfoton and residues were found in 10 out of 2700 surface water samples. Maximum concentrations were 0.002 μg/L and 0.007-0.041 μg/L in integrated streams/agricultural wells and urban/agricultural streams, respectively. There were no reported detections in about 2200 groundwater samples.

EPA's Pesticides in Groundwater Data Base (GWDB) (EPA 732-12-92-0001, 1992) and EPA's STORET data was also reviewed. EPA's GWDB showed no detects in 2430 wells from 11 states (limit of detection was 0.01 to 6.0 μg/L). However, the GWDB data showed that disulfoton was detected in six of 12 wells sampled in Virginia (0.04 to 2.9 μg/L) and in 14 of 26 wells (4.0 to 100 μg/L) sampled in Wisconsin. The data from Wisconsin was not quantity assured. The data from Virginia and Wisconsin wells show the potential contamination of wells in vulnerable areas and support the SCI-GROW modeling data.

4.3.4 DWLOCs for Acute and Chronic Exposure

The Drinking Water Level of Comparison (DWLOC) is the concentration of a pesticide in drinking water that is acceptable as a theoretical upper limit, in light of total aggregate exposure to the pesticide from food, water, and residential sources. DWLOCs have been calculated for acute dietary and chronic dietary exposure. For assessing human health risk, DWLOCs are compared to estimated environmental concentrations (EECs). When DWLOCs are greater than the EECs, the aggregate risk from food, water, and residential (if applicable) exposures is considered to be less than the Agency's level of concern.

4.3.4.1 Acute DWLOCs

The acute DWLOC values are shown in Table 8 below. The highest acutely exposed groups from food are children one to six years old and non-nursing infants less than one year old. The acute drinking water estimated concentration for surface water (58 μg/L) was greater than $DWLOC_{acute}$ for children one to six years and infants less than one year (23 μg/L). This indicates that acute exposure to disulfoton and residues in surface water may be a risk concern.

Table 8: DWLOC Values for Total Acute Dietary Exposure at the 99.9th percentile ($DWLOC_{acute}$)

Population	Acute PAD (mg/kg/day)	Food Exposure (mg/kg/day)	Max. Water Exposure (mg/kg/day)	$DWLOC_{acute}$ (μg/L)	PRZM/ EXAMS (μg/L[a])	SCI-GROW (μg/L)
US population	0.00250	0.000176	0.00232	81	58	3.2
Infants <1 yr/non nursing	0.00250	0.000237	0.00226	23	58	3.2
Children 1-6 yr	0.00250	0.000239	0.00226	23	58	3.2
Female (13+ yr/nursing)	0.00250	0.000117	0.00238	70	58	3.2
Seniors (55+ yr)	0.00250	0.000184	0.00232	81	58	3.2

[a]The peak water levels of 58 μg (disulfoton and cholinesterase inhibiting residues)/L from Tier 2 PRZMZ3/EXAMS (1-in-10 year values) model, page 15, Table 3b of the memorandum cited in section 4.4).

The default body weights and water consumption values used to calculate DWLOCs are as follows: 70 kg/2L (adult male), 60 kg/2L (adult female), and 10 kg/1L (children/infants). According to the August 1, 1999 Updated Interim Guidance for Incorporating Water Exposure into Aggregate Risk Assessments, the following formulas were used to calculate the acute DWLOCs.

$$DWLOC_{acute}\ (ug/L) = \frac{One-day\ water\ exposure\ \ (mg/kg/day) \times\ body\ \ weight\ (kg)}{Water\ consumption\ \ (L) \times\ 10^{-3}\ \ (mg/ug)}$$

Where;

$$One\text{-}day\ water\ exposure\ (mg/kg/day) =$$
$$[aPAD - Acute\ food\ exposure\ (mg/kg/day)]$$

4.3.4.2 Chronic DWLOCs

The chronic DWLOC values are shown in Table 9. The chronic drinking water estimated concentration for surface water (9.3 μg/L) exceeds the $DWLOC_{chronic}$ (1.2 to 4.4 μg/L) for all population subgroups. The chronic drinking water estimated concentration for groundwater (3.2 μg/L) exceeds the $DWLOC_{chronic}$ for children one to six years and infants less than one year. This indicates the chronic exposure to disulfoton and residues in drinking water may be a risk of concern.

Table 9: DWLOC Values for Total Chronic Dietary Exposure ($DWLOC_{chronic}$)

Population	Chronic PAD (mg/kg/day)	Food Exposure (mg/kg/day)	Max. Water Exposure (mg/kg/day)	$DWLOC_{chronic}$ (μg/L)	PRZM/ EXAMS (μg/L[a])	SCI-GROW (μg/L)
cPAD	0.000130	0	0.000130	4.5	9.3	3.2
US Population	0.000130	0.000003	0.000127	4.4	9.3	3.2
Infants <1 yr	0.000130	0.000001	0.000129	1.3	9.3	3.2
Children 1-6 yr	0.000130	0.000005	0.000125	1.2	9.3	3.2
Female (13+ yr)/nursing	0.000130	0.000002	0.000128	3.8	9.3	3.2

[a]The maximum mean of annual average concentration 9.3 μg (disulfoton and cholinesterase inhibiting residues)/L from PRZM/EXAMs model, tier 2 water assessment , page 15, Table 3b of the memorandum cited in section 4.4.

Chronic DWLOCs are calculated from chronic dietary (food) exposure and default body weights and default water consumption. According to the August 1, 1999 Updated Interim Guidance for Incorporating Water Exposure into Aggregate Risk Assessments, the following formulas were used to calculate the chronic DWLOCs.

$$DWLOC_{chronic}(ug/L) = \frac{Chronic\ water\ exposure\ (mg/kg/day) \times body\ weight\ (kg)}{Water\ consumption\ (L) \times 10^{-3}\ (mg/ug)}$$

Where;

$$Chronic\ water\ consumption\ (mg/kg/day) =$$
$$[cPAD - Chronic\ food\ exposure\ (mg/kg/day)]$$

4.4 Occupational/Residential Exposure

An occupational exposure assessment is required for an active ingredient if (1) certain toxicological criteria are triggered and (2) if there is potential exposure to handlers (mixers, loaders, applicators, etc.) during use or to persons entering treated sites after application is complete. Disulfoton meets both criteria.

Based on toxicological NOAELs and potential exposure and uses, the Agency has conducted exposure and risk assessments for occupational/residential handlers and postapplication workers. The margin of exposure (MOE), calculated for each occupational exposure scenario, is inclusive of total exposure (dermal and inhalation) and is calculated as $MOE = 1/[(1/MOE_{dermal}) + (1/MOE_{inhalation})]$.

4.4.1 Assumptions for Occupational Handler Exposure

An exposure assessment for each exposure scenario is developed where appropriate data are available, using the Pesticide Handlers Exposure Database (PHED) Version 1.1. PHED was designed by a task force of representatives from 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 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 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 the handler exposures to pesticides are primarily a function of activity (e.g., mixing/loading, applying), formulation type (e.g., liquids, 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 handled) may not accurately represent labeled uses in all cases. HED has developed a series of tables of standard unit exposure values for many occupational scenarios that can be utilized to ensure consistency in exposure assessments. The Revised Occupational and Residential Exposure Assessment, Appendix 6, summarizes the caveats and parameters specific to the surrogate data used for each scenario and corresponding exposure/risk assessment for disulfoton. Table 10 shows the range of MOEs for combined dermal and inhalation exposure. The range of the MOE in each scenario in Table 10 is the result of the different disulfoton label use rates possible by the handler. The highest MOE and the lowest MOE in Table 10, respectively represent the lowest and highest labeled use rate for that scenario.

Table 10: Occupational Handler Total Exposure (dermal and inhalation) to Disulfoton for Short- and Intermediate-Term Exposure with Baseline, PPE or Engineering Controls (EngC)

NOTE: An MOE<100 exceeds Agency's Level of Concern.
See Appendix 6 for additional detail about exposure and MOEs

Exposure Scenario (Scenario#)	Short-Term Exposure MOE			Intermediate-Term Exposure MOE		
	Baseline	PPE	EngC	Baseline	PPE	EngC
Mixer/Loader Risk						
Mixing/Loading Liquid Formulations (Emulsifiable Concentrates) for Aerial/ Chemigation Application (1a)	0.009-0.06	1.4-8.4	2.9-17	0.002-0.01	0.3-1.9	0.6-3.8
Mixing/Loading Liquid Formulations (Emulsifiable Concentrates) for Ground-boom Application (1b)	0.03-0.2	4.6-37	9.4-75	0.006-0.05	1.0-8.4	2.1-17
Mixing/Loading Liquid Formulations (Emulsifiable Concentrates) for Orchard Airblast Sprayer Application (1c)	0.08	12	25	0.02	2.8	5.6
Loading Granulars for Aerial Application (2a)	1.7-4.5	6.2-17	85-230	0.7-1.9	2.1-5.5	36-95
Loading Granulars for Tractor-Drawn Spreader Application (2b)	1.9-200	6.9-200+	93-1000	0.8-84	2.3-240	39-440
Applicator Risk						
Applying Sprays with a Fixed-Wing Aircraft (3)	No data See EC	No data See EngC	14-29	No data See EngC	No data See EC	3.3-6.5
Applying Granulars with a Fixed-Wing Aircraft (4)	No data See EngC	No data See EngC	3.0-8.0	No data See EngC	No data See EngC	2.0-5.4
Applying Sprays with a Helicopter (5)	No data See EngC	No data See EngC	42-84	No data See EngC	No data See EngC	8.8-18
Applying Granulars with a Helicopter (6)	No data	No data	No data	No data	No data	No data

Table 10: Occupational Handler Total Exposure (dermal and inhalation) to Disulfoton for Short- and Intermediate-Term Exposure with Baseline, PPE or Engineering Controls (EngC)

NOTE: An MOE<100 exceeds Agency's Level of Concern.
See Appendix 6 for additional detail about exposure and MOEs

Exposure Scenario (Scenario#)	Short-Term Exposure MOE			Intermediate-Term Exposure MOE		
	Baseline	**PPE**	**EngC**	**Baseline**	**PPE**	**EngC**
Applying Sprays with a Groundboom (7)	4.3-34	7.1-57	16-130	1.2-9.5	1.6-13	3.6-29
Applying Sprays to Orchards with an Airblast (8)	0.6	1.0	1.6	0.1	0.2	0.4
Applying Granulars with a Tractor-Drawn Spreader (9)	2.1-230	6.9-77	11-120	0.8-80	2.0-210	3.6-41
Mixer/Loader/Applicator Risk						
Loading/Applying Granulars Using a Belly Grinder (10)	0.3-1.3	0.2-0.8	NA	0.07-0.3	0.04-0.2	NA
Loading/Applying Granulars with a Push-Type Granular Spreader (11)	0.05-4.7	0.2-19	NA	0.01-1.0	0.04-4.0	NA
Loading/Applying Granulars by Hand, with a Spoon, Shaker Can, or a Measuring Scoop (12)	1.5	3.8	NA	0.3	0.8	NA
Applying Ready-to-Use Liquid as a Seed Treatment (13)	No data	No data	No data	No data	No data	No data
Flagger Risk						
Flagging Aerial Spray Applications (14)	5.7-11	7.5-15	15-30	1.4-2.9	1.6-3.3	3.3-6.6
Flagging Aerial Granular Applications (15)	9.7-26	21-55	9.9-26	2.7-7.2	5.0-16	3.3-8.9

Handler exposure assessments are completed by EPA using a baseline exposure scenario and, if required, increasing levels of risk mitigation. Progressively more methods of handler protection beyond baseline are added to achieve an appropriate margin of exposure (MOE), such as Personal Protective Equipment (PPE) and engineering controls (EngC). Adequate worker protection was not always achieved by any type of protection. The baseline scenarios generally represents a handler wearing long pants, a long-sleeved shirt, and no chemical-resistant gloves. PPE controls include, but are not limited to chemical resistant gloves, eye protection, dust /mist protection or respirator and extra clothing. EngC include closed systems (loading and packaging and/or closed tractor cabs or cockpits) and other means.

4.4.2 Occupational Handler Exposure and Characterization

The Agency has identified 15 different major exposure scenarios during mixing, loading and applying disulfoton products to agricultural crops and non-agricultural sites. The accepted range of application equipment and methods are covered in Appendix 6, in addition to the duration of handler exposure. The duration of exposure is covered by short-term (one day to one week), and intermediate-term (one week to several months) exposure scenarios. Disulfoton products are typically applied one to three times per season and at 20 to 42 day intervals.

The major routes of exposure to handlers are dermal and inhalation. The margins of exposure (MOE) are the ratio of the NOAELs to the exposure. MOEs are calculated for short-term and intermediate-term dermal and inhalation exposure and presented in Table 10 as combined MOEs for dermal and inhalation. Short-term and intermediate-term endpoints are presented in Section 3.2. There were no long-term occupational exposure scenarios. (See Appendix 6 for additional detail.)

4.4.3 Occupational Handler Risks of Concern

The acceptable occupational scenarios (MOE>100) given below are for short-term and intermediate-term exposure each with baseline and PPE protection and engineering controls in place. Most occupational scenarios exceed the Agency's level of concern (MOE<100). Of the 18 short-term and intermediate-term exposure scenarios (dermal and inhalation combined) listed in Table 10, 10 show marginally low MOEs between 70 and 100. For individual dermal MOEs and inhalation MOEs see Appendix 6. All occupational scenarios exceed the Agency's level of concern, except those listed below.

Calculations indicate that **none of the total short-term MOEs** are greater than 100 for baseline protection exposure scenarios **except** the following:

- (2b) loading granulars with a tractor-drawn spreader to nut (pecan) trees assuming an application rate of 3 lb ai/A, applied to 2 acres per day.

- (9) applying granulars with a tractor-drawn spreader to nut (pecan) trees assuming an application rate of 3 lb ai/A, applied to 2 acres per day.

Calculations indicate that **none of the total intermediate-term MOEs** are greater than 100 for baseline protection exposure scenarios.

Calculations indicate that **none of the remaining total short-term MOEs** are greater than 100 with additional PPE.

Calculations indicate that **none of the total intermediate -term MOEs** are greater than 100 **with additional PPE except** the following:

- (2b) loading granulars with a tractor-drawn spreader to nut (pecan) trees assuming an application rate of 3 lb ai/A, applied to 2 acres per day.

- (9) applying granulars with a tractor-drawn spreader to nut (pecan) trees assuming an application rate of 3 lb ai/A, applied to 2 acres per day.

Calculations indicate that **none of the total short-term** MOEs are greater than **100** for scenarios with **engineering controls** in place **except** the following:

- (2a) loading granulars for aerial application using a 1.0 lb ai/A or less application rate.

- (2b) loading granulars for tractor-drawn spreader application to agricultural crops at application rates of 4 lb ai/A or less. MOEs are greater than 100 also for loading of granulars for application to non-bearing fruit trees and to flowers and groundcovers using a tractor-drawn spreader.

- (7) applying with a groundboom to agricultural crops using an application rate of 0.5 lb ai/A.

- (9) applying granulars with a tractor-drawn spreader to agricultural crops at 0.75 lb ai/A and to flowers and groundcover using an application rate of 28.6 lb ai/A.

Calculations indicate that **none of the total intermediate-term** MOEs are greater than **<u>100</u>** for scenarios with **engineering controls** in place **except** the following:

- (2b) loading granulars for tractor-drawn spreader application to agricultural crops at application rate of 1 lb ai/A or less. MOEs are greater than 100 also for loading of granulars for application to non-bearing fruit trees and to flowers and groundcovers using a tractor-drawn spreader.

4.4.4 Data Gaps

As noted below, several of the exposure scenarios could not be assessed due to lack of PHED surrogate data. Data gaps exist for the following scenario:

- (6) - no PHED data exist for applying granulars from helicopters.

- (16) - no PHED data exist for applying ready-to-use liquid as a seed treatment.

4.4.5 Data Quality and Confidence in Assessment

Several issues must be considered when interpreting the occupational exposure risk assessment. Confidence in the exposure data is also listed in Appendix 6, as low (L), medium (M) or high (H). These include:

- Several handler assessments were completed using “low quality” PHED data due to the lack of a more acceptable data set.

- Several generic protection factors were used to calculate handler exposures. These protection factors have not been completely evaluated and accepted by HED.

- Factors used to calculate daily exposures to handlers (e.g., acres treated per day and gallons of liquid applied) are based on the best professional judgement, due to a lack of pertinent use data.

4.4.6 Postapplication Exposure

Postapplication exposure potential occurs to individuals entering treated areas for harvesting nut trees (pecans); harvesting low-growing field crops; weeding and scouting and other non-harvesting activities associated with low-growing crops; and transplanting, harvesting and pruning ornamentals. EPA estimates that a 48-hour reentry interval (REI), based on the acute toxicity category (I), and is adequate to protect field workers when 4.0 lb ai/A or less has been applied as a disulfoton spray or granules to the field. For use rates that exceed 4.0 lb ai /A, minimum reentry times of 28 to 36 days are estimated using standard values (Table 11). The assumptions made would be expected to bracket the reentry exposure levels from disulfoton used on these crops.

This consideration is based on the following: (1) Use of high rates directly on soil and that often soil incorporated (either mechanically or by watering in) occurs and that high application rates may be rarely used and (2) the use of a residue fraction that is retained on the foliage and available for transfer is likely to be substantially less than the 20 percent used. Additional data are required to further refine the post application exposure assessment.

Based on these activities, four representative scenarios were evaluated using surrogate dislodgeable foliar residue data and assumptions about transfer of residues to skin. The surrogate assessments presented in Table 11 are based on the applications rates on disulfoton labels that are recommended for field crops, nut trees and ornamentals.

Additional details, default assumptions and formulas for the calculations for the dislodgeable foliar residues and reentry times are presented in Appendix 6.

Table 11: Disulfoton Intermediate-Term Surrogate Occupational Postapplication Assessment (Range Finder) for high Application Rates

Application Rate (lb ai /A)	DAT[a]	DFR (μg/cm^2)[b]	Dermal Dose (mg/kg/day)	MOE
8	28	0.006	0.0002	130
28.6	32	0.006	0.0003	110
102	36	0.0007	0.0003	100

[a]DAT is "days after treatment."
[b]Initial DFR = Application rate x Conversion factor (lb ai/A = 11.209 μg/cm^2) x fraction of initial ai retained on foliage.

4.4.7 Human Incidence Information

Human incidence data contained in a memorandum from Jerome Blondell to Jonathan Becker of HED (3/25/1998), Review of Disulfoton Incidence Reports, show that disulfoton was 11th among the 28 pesticides reported (1982-1989) with the highest incidence rates and had the highest ratio for cases when the pesticide was considered the primary cause of poisoning of field workers per 1000 applications. Disulfoton ranked third on percentage of occupational Poison Control Center cases requiring hospitalization and fourth among these 28 pesticides studied on percentage of occupational cases with life-threatening symptoms. Death (including suicides and possible homicides) confounded by misuse is known to infrequently occur; however, no other permanent disability has been adequately documented. The report does not indicate the frequency or proportion of incidences related to morbidity, to labeled uses, or misuse.

4.5 Residential Exposure

4.5.1 Handler

Disulfoton is applied one to three times per season and thus individual handlers would mostly be exposed short-term. Short-term exposure scenarios were used to calculated anticipated residential exposure (Table 12). Although short-term exposure is defined as one day to one week, the dermal and inhalation toxicity data used in the calculations covers up to three weeks of daily exposure and is considered a conservative estimate of residential exposure. An MOE of 100 or greater is below the Agency's level of concern for residential exposure. Exposure to granular formulations were evaluated, since only granular formulations are recommended for residential use.

The residential risk was shown to range from MOEs of 0.002 to 1,900 (Table 12). Only two types of activities had MOEs below the Agency's level of concern for the lowest application rates only, and these were: (1) loading /applying granulars with a push type spreader to flower gardens at the lower rates of 0.005 lb ai/1,000 ft^2 (MOE=1,900), and (2) using the same type of equipment at the lowest rate of 0.00032 lb ai/4 ft shrub (MOE=1,200). Two other activities show marginally low MOEs. These were (1) loading /applying granulars with a push type spreader to flower gardens at the lower rates of 0.1 lb ai/1,000 ft^2 (MOE=93), and loading and applying granulars with a push type spreader at the labeled use rate of 0.00188 lb ai/bush to 50 rose bushes (MOE=99). All other residential activities showed MOEs ranging from 0.002 to 37 (Table 12). Table 12 lists MOEs for dermal and inhalation exposure combined. For individual dermal MOEs and inhalation MOEs see Appendix 6.

The anticipated residential use patterns and current labeling indicate several major exposure scenarios based on the types of equipment that potentially can be used to make disulfoton applications. These scenarios include: (1) loading/applying

granulars with a belly grinder; (2) loading/applying granulars with a push type spreader; (3) loading/applying granulars with a spoon, shaker can, measuring scoop, or by hand; (4) application of insecticidal spikes.

4.5.2 Residential Handler Exposure Scenarios-Data and Assumptions

Residential handler exposure assessments were completed by HED using a baseline exposure scenario. PHED values used to estimate daily unit exposure were taken from *Standard Operating Procedures (SOPs) for Residential Exposure Assessments*, document dated December 1997. The caveats and parameters specific to surrogate data used for each scenario and corresponding exposure/risk assessment are detailed in Appendix 6.

Data Quality

The quality of the data used in the residential and non-occupational risk assessment is ranked of low confidence category for push type granular spreaders. Factors used to calculate daily exposures to handlers (e.g., square footage treated per day, number of pots treated per day and number of tree or shrubs treated per day) are best professional judgement due to a lack of pertinent data.

Data Gaps

No satisfactory data exists for applying insecticidal spikes to roses or ornamental shrubs and trees.

Table 12: Residential Handler Short-term Risks from Disulfoton at Baseline				
Exposure Scenario (Scenario #)	**Crop Type or Target [a]**	**Amount Handled Per Day [b]**	**Application Rate**	**Baseline Total Short-Term MOE[c]**
Mixer/Loader/Applicator Risks				
Loading/Applying Granulars with a Belly Grinder (1)	Flower/Veg Gardens (pre-planting)	10,000 ft.^{2}	0.2 lb ai/1000 ft^2	0.1
			0.1 lb ai/1000 ft^2	0.3
Loading/Applying Granulars with a Push Type Spreader (2)	Roses	50 bushes	0.00188 lb ai/bush	99
	Vegetable Gardens	10,000 ft.^{2}	0.1125 lb ai/1,000 ft^2 [h]	8.2
			0.0313 lb ai/1,000 ft^2 [h]	30
	Flower Gardens	1,000 ft.^{2}	0.3 lb ai/1,000 ft^2	31
			0.1 lb ai/1,000 ft^2	93
			0.005 lb ai/1,000 ft^2	1,900
	Ornamental Shrubs/ Small Trees	25 shrubs	1.32 lb ai/4 ft. shrub	0.3
			0.01 lb ai/4 ft. shrub	37
			0.00032 lb ai/4 ft. shrub	1,200
Loading/Applying Granulars with a Spoon, Shaker Can, Measuring Scoop, or by Hand (3)	Roses	50 bushes	0.00188 lb ai/bush	0.7
	Vegetable Gardens	10,000 ft.^{2}	0.1125 lb ai/1,000 ft^2 [h]	0.06
			0.0313 lb ai/1,000 ft^2 [h]	0.2
	Flower Gardens	1,000 ft.^{2}	0.3 lb ai/1,000 ft^2	0.2
			0.1 lb ai/1,000 ft^2	0.6
			0.005 lb ai/1,000 ft^2	13
			1.32 lb ai/4 ft. shrub	0.002
	Ornamental Shrubs/ Small Trees	25 shrubs	0.01 lb ai/4 ft. shrub	0.3
			0.00032 lb ai/4 ft. shrub	8.1
	Potted Plants	20 pots	0.00011 lb ai/6" pot	29

Table 12: Residential Handler Short-term Risks from Disulfoton at Baseline				
Exposure Scenario (Scenario #)	**Crop Type or Target [a]**	**Amount Handled Per Day [b]**	**Application Rate**	**Baseline Total Short-Term MOE[c]**
Application of Insecticidal Spikes (4)	Roses/Trees	No Data	No Data	No Data

[a]Crop Type or Target provides a general description of the intended use of various products containing disulfoton. Separate categories are presented because of the distinct differences in application rates and acres treated.
[b]Amount Handled Per Day values are from default estimates of square footage or number of pots treated a single day for each exposure scenario of concern.
[c]Total Short-term MOE = 1/ [(1/ Short-term Dermal MOE) + (1/ Short-term Inhalation MOE)].

4.5.3 Postapplication Residential Exposure and Risk

Potential postapplication exposure from residential use of the granular product can occur during transplanting garden or house plants, and weeding treated flowers, ornamental shrubs, and trees. Potential exposure can occur from non-harvest activities such as weeding home vegetables, and from incidental soil ingestion by toddlers (hand-to-mouth exposure).

The Agency has no data upon which to assess postapplication contact with treated soil through activities such as weeding, hoeing, and transplanting home ornamentals, vegetable crops, and house plants. However, postapplication risks for adult homeowners were estimated to be low.

Exposure to toddlers was assessed using surrogate data. Exposure to toddlers (hand-to-mouth) in treated vegetable and flower gardens at the maximum application rates for these scenarios show MOEs of 230 and 610, respectively. Lower rates of application would show even higher MOEs. No data were available to assess exposure to toddlers (hand-to-mouth) for shrubs and small tree areas treated with disulfoton by residential handlers.

In calculating postapplication toddler exposure, the intermediate-term NOAEL of 0.03 mg/kg/day was used rather than short-term NOAEL of 0.4 mg/kg/day because some reentry activity was considered to be longer than one to seven days and to be conservative. The MOE for toddlers ingesting soil at vegetable and flower garden application sites (at the lowest application rate) showed an acceptable MOE greater than 100.

4.5.4 Potential Spray Drift

This assessment reflects the Agency's current approaches for completing residential exposure assessments based on the guidance provided in the *Draft: Series 875-Occupational and Residential Exposure Test Guidelines, Group B-Postapplication Exposure Monitoring Test Guidelines (7/24/97 Version)*, the *Draft: Standard Operating Procedures (SOPs) for Residential Exposure Assessment (12/11/97 Version)*, and the *Overview of Issues Related to the Standard Operating Procedures for Residential Exposure Assessment* presented at the September 1999 meeting of the FIFRA Scientific Advisory Panel (SAP). The Agency is, however, currently in the process of revising its guidance for completing these types of assessments and expanding the scope of the residential exposure assessments by developing guidance for characterizing exposures from other sources already not included such as from spray drift, residential residue track-in, exposures to farm worker children, and exposures to children in schools. Modifications to this assessment for disulfoton shall be incorporated as updated guidance becomes available and it is feasible from a regulatory perspective.

5.0 AGGREGATE RISK (FOOD, WATER AND RESIDENTIAL)

The Food Quality Protection Act amendments to the Federal Food, Drug, and Cosmetic Act (FFDCA, Section 408(b)(2)(A)(ii)) require for establishing a pesticide tolerance "that there is reasonable certainty that no harm will result from aggregate exposure to pesticide chemical residue, including all anticipated dietary exposures and other exposures for which there is reliable information." Aggregate exposure will typically include exposures from food, drinking water, and residential uses of a pesticide.

The aggregate risk estimate to disulfoton has addressed exposure from dietary (food) sources, drinking water, and residential uses. Acute and chronic dietary food risks are below the Agency's level of concern (<100 percent aPAD/cPAD). All of the residential use scenarios specified on the label exceed the Agency's level of concern (i.e., MOE<100) at the maximum application rate, except for roses which are at the level of concern/no concern (MOE=99). PRZM/EXAMS estimates[3] of exposure to disulfoton in surface water exceed the Agency's level of concern (i.e., DWLOCs<EECs). Therefore, any aggregation of exposure from residential uses and drinking water with food exposure would only further increase the risk even higher than the Agency's level of concern.

[3]Since the PRZM/EXAMS model estimates are greater than the SCI-GROW model estimates, DWLOCs are compared to the PRZM/EXAMS estimates only.

6.0 ENDOCRINE MODULATION

The Food Quality Protection Act requires that EPA develop a screening program to determine whether certain substances (including all pesticides and inerts) "may have an effect in humans that is similar to an effect produced by a naturally occurring estrogen, or such other endocrine effect...." EPA has been working with interested stakeholders, including other government agencies, public interest groups, industry and research scientists to develop a screening and testing program as well as a priority setting scheme to implement this program. The Agency's proposed Endocrine Disrupter Screening Program was published in the Federal Register of December 28, 1998 (6 3 FR 71541). The Program uses a tiered approach and anticipates issuing a Priority List of chemicals and mixtures for Tier 1 screening in the year 2000. As the Agency proceeds with implementation of this program, further testing of disulfoton and its end-use products for endocrine effects may be required.

7.0 CUMULATIVE EXPOSURE AND RISK

It has been determined that organophosphates (OPs) share a common mechanism of inhibiting cholinesterase. As required by FQPA, cumulative assessment will need to be conducted to evaluate the risk from food, water and non-occupational exposure resulting from all uses of organophosphates. The Agency is in the process of formulating guidance for conducting cumulative risk assessments. When the guidance is finalized, disulfoton and other ChE-inhibiting compounds (carbamates and organophosphates) will be revisited to assess the cumulative effects of exposure to multiple cholinesterase inhibiting compounds.

8.0 REQUIRED DATA

The only toxicity study required is from a general data-call-in for a developmental neurotoxicity study (Guideline# 870.6300), for which disulfoton was included. There are requirements for product chemistry and several for tolerance assessments and recommendations for tolerance revocation (See the Appendix 5: Residue Chemistry Considerations for the Disulfoton RED).

***Data needs for Product Chemistry**:*

- Guideline #830.1750 for EPA Reg. No. 3125-183
- Guideline #830.1800 for EPA Reg. No. 3125-183
- Guideline #830.7050 for EPA Reg. No. 3125-183
- Guideline #830.1800 for EPA Reg. No. 3125-158
- Guideline #830.1800 for EPA Reg. No. 3125-128

Additional data needs for residue chemistry are listed in Appendix 5.

Data needs for Occupational Assessment:

Occupational exposure data is necessary for applying granulars from helicopters and for applying ready-to-use liquid as a seed treatment because no PHED data exist for these scenarios. In addition, the Agency has no data on exposure from the use of disulfoton spikes for tree treatment.

9.0 CODEX

The Codex MRLs are expressed in terms of the sum of disulfoton, demeton-S, and their sulfoxides and sulfones expressed as disulfoton. Some US tolerance are still expressed in terms of demeton-S. However, since the molecular weight of disulfoton is only six percent lower than demeton-S, the difference is small. Codex MRLs and the U.S. tolerances will be compatible when the U.S. tolerance expression is revised to include disulfoton, its oxygen analog, and their sulfoxides and sulfones, calculated as disulfoton.

10.0 APPENDICES

Appendix 1: Toxicology Chapter for the Disulfoton RED (David G. Anderson)

Appendix 2: The Hazard Identification Assessment Review Committee Report for Disulfoton (Revisit) (David G. Anderson).

Appendix 3: The FQPA Safety Factor Committee Report on Disulfoton (Brenda Tarplee).

Appendix 4: The Revised Disulfoton: Acute and Chronic Dietary Risk Assessment (Includes MRID # 44821701 & 44821702, Chem. No. 032501; William O. Smith)

Appendix 5: Product Chemistry and Residue Chemistry Chapters for the Disulfoton RED (John Abbots/Ken Dockter)

Appendix 6: Occupational/Residential Exposure Chapter for the Disulfoton RED (Jonathan Becker) *and* Memorandum from Jerome Blondell to Jonathan Becker of HED (3/25/1998): Review of Disulfoton Incidence Reports (Jerome Blondell)