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MEMORANDUM

SUBJECT: **Dicrotophos** (List A, Reregistration Case No. 0145). HED Risk Assessment for Reregistration Eligibility Document (RED.) Chemical No: 035201; DP Barcode: D276599;

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Attached is a revision of Health Effects Division's (HED's) revised risk assessment of dicrotophos for purposes of issuing a Reregistration Eligibility Decision (RED) Document for this active ingredient.

This risk assessment document updates the April 5, 2000 Dicrotophos Risk Assessment by incorporating data from new toxicity studies submitted by the registrant after April, 2000. All relevant disciplinary science chapters and supporting documents have been revised to reflect new toxicity data.

Report of the Hazard Identification Assessment Review Committee. Sanju Diwan & Abdallah Khasawinah (October 10, 2001 HED DOC NO 014694)
Report of the FQPA Safety Factor Committee. B. Tarplee (October 24, 2001 HED DOC NO 014699)
Product & Residue Chemistry Chapter. G. Otakie (June 8, 1999, D241592)
Agriculutural and Occupational Exposure Assessment. T. Leighton (October 31, 2001, D241956)
Dietary Exposure and Risk Estimates for Reregistration. B. Daiss (October 30, 2001 D278883)
Incident Report. M. Spann and J. Blondell, Ph.D (July 9, 1998, D247490)
Environmental Fate and Effects Water EECs. K. McCormack (November 4, 1998) and J Carleton (October 24,2001 D278533)

RDI: BRSrSci: SVHummel: 11/0/01

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1.0 EXECUTIVE SUMMARY

The Health Effects Division (HED) has conducted a human health assessment for the active ingredient dicrotophos (dimethyl phosphate of 3-hydroxy-N,N-dimethyl-cis-crotonamide) for the purpose of making a reregistration eligibility decision. In conducting its assessment, HED evaluated the toxicology, residue chemistry, and exposure data bases for dicrotophos and determined that the data are adequate to support a reregistration eligibility decision. HED assessed acute and chronic (non-cancer)dietary risks and occupational risks. There are no residential/homeowner uses of dicrotophos.

Dicrotophos is a contact, systemic acaricide/insecticide registered for use on cotton [40 CFR §180.299]. The only dicrotophos end-use formulation currently registered is a water-miscible formulation (Bidrin®) which may be applied foliarly to established cotton plants. At this time products containing dicrotophos are intended for occupational use only. It is classified as Restricted Use and may be purchased and used only by certified applicators or persons under their direct supervision.

Hazard Identification

The toxicology data base for dicrotophos has been reevaluated based on recently submitted developmental, dermal and neurotoxicity studies (HED DOC NO 014694 S. Diwan, 10/10/01). This risk assessment document has been updated to reflect revisions to toxicity endpoints based on the new studies and reevaluation of the existing data base.

Dicrotophos is an organophosphate (OP) insecticide; its mode of toxic action is via the inhibition of cholinesterase (ChE) activity. In all studies in which ChE was measured, the Lowest Observed Adverse Effect Level (LOAEL) was based on plasma, red blood cell (RBC) or brain ChE inhibition. In some studies, including both short-term and chronic administration, all three effects were seen at the LOAEL. The NOAEL was not established. Dicrotophos is a potent cholinesterase inhibitor to rodents, rabbits and dogs at very low doses. Female rats are more sensitive than males in acute oral studies. The rat is also more sensitive than the mouse in both acute and chronic studies.

Dicrotophos is acutely toxic to rats by the oral and dermal routes of exposure. No inhalation data are available. Primary eye and skin irritation fall into Toxicity Categories II and IV, respectively. Dicrotophos is a strong dermal sensitizer. There was no evidence of delayed neurotoxicity in the hen study. Evidence of ChE inhibition was observed in several of the studies, however there was no evidence of alterations in structural neuropathological (gross and histopathology) parameters. In a subchronic neurotoxicity study in rat, decreases in body weight and food consumption, and cholinesterase inhibition were observed.

There was no evidence of prenatal developmental toxicity or increased fetal susceptibility in rats or rabbits. In the 2-generation reproduction study, dietary administration of dicrotophos

caused severe effects on pups (reduced number of pups/litter) at a dose that caused toxicity in parental animals (reduced weight gain and food consumption) providing qualitative evidence of susceptibility.

Dicrotophos was nonmutagenic *in vitro salmonella typhimurium* assay and *in vivo* micronucleus assay when tested up to cytotoxic doses. However, it induced positive dose dependent gene mutations in mouse lymphoma L51784 cell cultures.

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The carcinogenicity data demonstrated that dicrotophos produced an increase in thyroid follicular cell adenomas in male mice. There was no evidence of carcinogenicity in the rat. The Cancer Assessment Review Committee (CARC) concluded that there is "Suggestive evidence of carcinogenicity, but not sufficient to assess human carcinogenic potential". The evidence from animal data is suggestive of carcinogenicity, which raises a concern for carcinogenic effects, but is judged not sufficient for a conclusion as to human carcinogenic potential. Such evidence includes increased tumor incidence only in mice.

Based on newly submitted toxicity studies and reevaluation of existing studies, the FQPA Safety Factor Committee recommended that the FQPA safety factor for dicrotophos be reduced to 3x for the chronic endpoint and to1x for the acute endpoint (HED DOC NO 014699, B. Tarplee).

The core toxicity study requirements, as well as additional environmental fate/effects, residue, drift and re-entry data requirements were imposed in a Data Call-In (issued in 1991). Additional DCIs imposed human incident data requirements (1993) and worker exposure requirements (1995). The available toxicology data partially satisfy current FIFRA Test Guideline requirements. Existing data gaps include: 1) an acute inhalation toxicity study for labeling purposes; and 2) a 28-day inhalation study in rats.

Drinking Water Exposure

Estimates of environmental concentrations of dichrotophos in surface water sources of drinking water have been updated for this assessment. Using the Index Reservoir (IR) and Percent Crop Area (PCA) modifications to the PRZM /EXAMS models and available environmental fate data for dicrotophos, the Environmental Fate and Effects Division (EFED) calculated Tier II Estimated Environmental Concentrations (EECs) for dicrotophos in surface water following application of the chemical to cotton. The calculated acute or peak EEC for surface water is 2.56 ppb. The chronic (one in 10 year upper 10^{th} percentile) surface water EEC is 0.23 ppb. Using the SCI-GROW model, EFED calculated an EEC of 0.005 ppb for dicrotophos in ground water.

Non-Occupational Exposure And Risk Assessments

HED conducted a revised acute and chronic dietary (food) exposure analyses using the Dietary Exposure Evaluation Model (DEEM™) and revised toxicity endpoints for dicrotophos. In the acute dietary assessment, exposure was compared to the acute Population Adjusted Dose

(aPAD) based on the acute reference dose (RfD) and a 1x FQPA Safety Factor. In the chronic dietary assessment, exposure was compared to the chronic PAD based on the chronic RfD and retention of a 3x FQPA Safety Factor. HED considers dietary residue contributions greater than 100% of the PAD to be of concern. The acute and chronic analyses (Tier 3 for each analysis) are refined estimates using anticipated residues from field trial data, and percent of crop treated data from Biological Economic Analysis Division (BEAD). No monitoring data from USDA's Pesticide Data Program (PDP) or FDA's Surveillance Monitoring program were available for dicrotophos.

Acute dietary exposures (mg/kg/day) estimates at the 99.9 percentile were below HED's level of concern for all subpopulations. The subgroup with the highest estimated exposure was children 1-6 yrs. Their exposure was estimated at 0.000004 mg/kg/day resulting in a risk estimate of 0.27% of the acute population adjusted dose (aPAD). The general U.S. Population's acute dietary exposure and risk estimates were 0.000002 mg/kg/day and 0.12% of the aPAD, respectively.

Chronic dietary exposures (mg/kg/day) estimates are below HED's level of concern for all subpopulations. The subgroup with the highest estimated exposure was children 1-6 yrs their estimated exposure was < 0.000001 mg/kg/day resulting in a risk estimate of 0.9% of the chronic population adjusted dose (cPAD.) The general U.S. Population's chronic dietary exposure and risk estimates were <0.000001 mg/kg/day and 0.1% of the cPAD, respectively.

Based on the above-calculated acute exposure from food, HED has calculated the acute Drinking Water Level of Comparison ($DWLOC_{acute}$) for acute dietary exposures to dicrotophos. The DWLOC is the concentration in drinking water which, when combined or aggregated with exposures through food, would result in an aggregate exposure which is acceptable. In other words, it is the theoretical concentration of a pesticide in drinking water which would be an acceptable upper limit in light of the total aggregate exposure to that pesticide through all pathways. If model-based estimated concentrations in ground and surface waters are less than the $DWLOC_{acute}$, OPP can conclude with reasonable certainty that aggregate exposure through food and drinking water do not exceed HED's level of concern.

HED's calculated $DWLOC_{acute}$ is 17 ppb (based on the most highly exposed subgroup, children 1-6). Environmental Fate and Effects Division's (EFED's) model-based estimates for maximum concentrations in surface and ground water are 2.56 ppb and 0.005 ppb, respectively. Since the model-based estimate for concentrations in surface water and groundwater are below HED $DWLOC_{acute}$ (17 ppb), HED concludes with reasonable certainty that aggregate exposure to dicrotophos through food and surface water and food and ground water will not result in unacceptable exposure and risk.

Based on the above-calculated chronic exposure from food, HED has also calculated the DWLOC for chronic dietary exposures to dicrotophos. HED's revised calculated $DWLOC_{chronic}$ is 0.2 ppb (based on the most exposed subgroup, children 1-6). EFED's model-based estimates for average concentrations of dicrotophos in surface and ground water are 0.2 ppb and 0.005 ppb, respectively. Since the model-based estimate for concentrations in surface water (0.2 ppb)

equals HED's $DWLOC_{chronic}$ of 0.2 ppb, HED concludes with reasonable certainty that residues of dicrotophos in food and surface water result in levels of aggregate exposure do not exceed HED's level of concern. Model estimates for dicrotophos in ground water are below $DWLOC_{chronic}$, therefore, HED concludes that aggregate exposure to dicrotophos through food and ground water will not result in unacceptable exposure and risk. It is important to note that calculated surface water values for dicrotophos are within the range of concentrations recently detected in surface water in the Mississippi River alluvial plane.

Aggregate (Food, Water and Residential) Exposure and Risk Estimate

Aggregate risk is estimated by combining dietary (food and water) and residential exposures. Dicrotophos has no uses that could result in residential exposure, therefore, the aggregate risk estimate will be based on the dietary exposure from food and water only, for the most highly exposed population subgroups and the general population. Details concerning the assumptions used in deriving exposure estimates and risk characterizations were discussed previously in this document.

Occupational Exposure Summary and Characterization of Risk

The occupational exposure assessment has been updated based on newly submitted toxicity data and reevaluation of existing data. A revised dermal toxicity endpoint based on a new 21-day dermal rat study was used to assess dermal risks from dicrotophos. In addition, a discussion of a dicrotophos-specific handler study identified by the registrant is included in the updated occupational assessment.

There are no residential or non-occupational uses for dicrotophos; therefore residential exposures are not likely, nor are residential postapplication exposures expected. There is potential for spray drift during aerial application, however, HED does not currently have an approved method of assessing this scenario. Incident data do not indicate that spray drift is a problem.

Margins of exposures (MOEs) for occupational exposure risk assessments: The target MOE is 300 for both dermal and inhalation exposure risk assessments and includes the conventional factor of 100 and an additional factor of 3 for the use of a LOAEL for all risk assessments. Since the dermal and inhalation endpoints are based on cholinesterase inhibition, an aggregate (dermal and inhalation) risk assessment is required.

Surrogate data, which included chemical specific data, from the Pesticide Handlers Exposure Database (PHED) were used to estimate the exposures. The data in PHED for the typical agricultural scenarios assessed (i.e., aerial and groundboom) are representative of the cotton use. The results of the short-term handler assessment of aggregated risks indicate that 7 of the 15 scenarios have total MOEs greater than 300. All other short term risks remain at levels of concern with MOE's ranging from 26 to 270 with engineering control protection. The results of

the intermediate-term handler aggregate risks indicate that six scenarios have total MOEs greater than 300. All the remaining intermediate-term MOEs are below 300 and range 18 to 270 with engineering control protection.

Chemical-specific dislodgeable foliar residue (DFR) data were submitted in support of the postapplication assessment. However, worker reentry exposure data were not available. Therefore, transfer coefficients were estimated for scouting, irrigating, hand weeding, and hand harvesting and hoeing activities using revised transfer coefficients from the August 2, 2000, HED Science Advisory Council for Exposure Policy (#3.1).

Results of the postapplication assessment for short- and intermediate-term dermal exposures indicate that for hand harvesting activities, postapplication MOE's are greater than 300 at day 8; for "late-season" irrigating, scouting, and hand weeding activities, postapplication MOEs are greater than 300 at day 6; and for "early-season" irrigating, scouting, and hand weeding activities, MOEs are greater than 300 on day 0. There are no data upon which to assess exposures and risks resulting from mechanical harvesting activities; however, Policy #3.1 states that "significant worker exposure is possible from [mechanical harvesting cotton] activity".

The handler and postapplication assessments are believed to be reasonable high end representations of dicrotophos uses. There are, however, many uncertainties in these assessments. The uncertainties include but are not limited to the following:

- exposure of an intermediate-term duration to assess all uses;
- extrapolating exposure and DFR data by the amount of active ingredient handled or applied; and
- application timing in comparison to actual potential postapplication exposure scenarios.

These uncertainties are inherent in most pesticide exposure assessments. The conservative nature of the assessments, however, is believed to be protective of the handlers and postapplication workers.

Conclusions

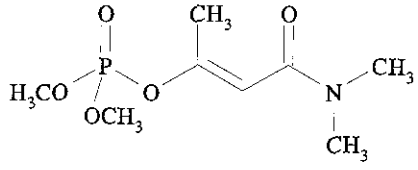
The submission of additional toxicity data resulted in reduced uncertainty regarding conclusions drawn from the revised dicrotophos risk assessment. The previous 10,000 fold uncertainty/safety factor has been reduced to 900 for the chronic dietary exposure endpoint (10x for inter-species, 10x for intra-species, 3x for use of a LOAEL, and 3x for FQPA) and to 300 (10x for inter-species, 10x for intra-species, and 3x for use of a LOAEL) for the acute dietary endpoints and MOEs of 300 for all occupational exposure endpoints. Use of these smaller uncertainty factors result in PADs and MOEs that provide greater allowances for drinking water calculations relative to the previous assessment. Reduction in the uncertainty factors should also result in smaller differences between estimated occupational risk and target MOEs, given that all other factors remain the same.

The anticipated residues used in the dietary assessment were taken from field trials rather than monitoring data because no monitoring data are available for cotton commodities. Therefore, it was assumed that the application rate was 1x with the shortest allowable pre-harvest interval (i.e. the maximum label rate.) This results in residues more representative of "at the farmgate", than the dinner plate. Field trial residues do not consider degradation and removal of residues through transport, distribution, washing, cooking, and peeling. Therefore, the dietary exposure estimates are conservative, upper bound estimates.
Dicrotophos has no uses that would legally result in residential exposure, therefore, the aggregate risk estimate was based on the dietary exposure from food and water only, for the most highly exposed population subgroups and the general population as appropriate.

Comparing the revised acute and chronic surface water EECs to the revised acute and chronic DWLOCs, HED can conclude with reasonable certainty that residues of dicrotophos in food and surface water result in levels of aggregate exposure at or below HED's level of concern. Model estimates for dicrotophos in ground water are below both $DWLOC_{acute}$ and $DWLOC_{chronic}$, therefore, HED concludes that with reasonable certainty that aggregate exposure to dicrotophos through food and ground water will not result in unacceptable exposure and risk.

Short-term occupational handler total risks resulted in MOEs lower than the target MOE 300 for 8 of the 15 scenarios indicating a potential risk concern. These MOEs ranged from 26 to 270 with engineering control protection. For the intermediate-term occupational handler, 9 of the 15 total risks scenarios resulted in MOEs below 300. MOEs of concern ranged from 18 to 270 with engineering control protection. MOEs for short- and intermediate-term dermal postapplication exposures are greater than the target MOE of 300 at day 8 for hand harvesting, greater than 300 at day 6 for "late-season", and greater than 300 at day 0 for "early-season" activities. Data are not available for assessment of risks from mechanical harvesting activities. However, based on HED's Science Advisory Council Exposure Policy, significant worker exposure is possible from these activities.

2.0 PHYSICAL/CHEMICAL PROPERTIES CHARACTERIZATION



Empirical Formula:	$C_8H_{16}NO_5P$
Molecular Weight:	237.21
CAS Registry No.:	141-66-2

Dicrotophos is a mixture of the E- and Z-isomers in which the E-isomer is pesticidally active. Technical dicrotophos is a yellow to dark amber liquid at room temperature with a

boiling point of 111-112 C at 0.022 mm Hg (399 C at 760 mm Hg), density of 1.19-1.22 g/mL at 20 C, octanol/water partition coefficient (K_{ow} of PAI) of 2.445 (E-isomer) and 0.000481 (Z-isomer), and vapor pressure of 2.2 x 10^{-5} mm Hg at 20° C and/or 2.9 mPa at 20 C. Dicrotophos is miscible (mixable in all proportions) with water, acetone, alcohol, acetonitrile, chloroform, methylene chloride, and xylene. Dicrotophos is only slightly soluble in kerosene and diesel fuel.

3.0 HAZARD CHARACTERIZATION

3.1 Hazard Profile

Dicrotophos is an organophosphate (OP) insecticide whose mode of toxic action is the inhibition of cholinesterase (ChE). In all studies in which ChE was measured, the Lowest Observed Adverse Effect Level (LOAEL) was based on plasma, RBC and brain ChE inhibition. The NOAEL was not established. Dicrotophos is a potent ChE inhibitor to rodents, rabbits and dogs at very low doses. Female rats are more sensitive than males in acute oral studies. The rat is also more sensitive than the mouse in both acute and chronic studies.

Dicrotophos is acutely toxic to rats by the oral and dermal routes of exposure. No inhalation data are available. Primary eye and skin irritation fall into Toxicity Categories II and IV, respectively. Dicrotophos is a strong dermal sensitizer. ChE inhibition was observed in several of the studies, however there was no evidence of alterations in structural neuropathological (gross and histopathology) measurements. A subchronic neurotoxicity study was conducted in rat in which dicrotophos produced decreases in body weight and food consumption, and cholinesterase inhibition.

There was no evidence of prenatal developmental toxicity or increased quantitative or qualitative fetal susceptibility in rats. In the 2-generation reproduction study dietary administration of dicrotophos caused severe effects on pubs (reduced number of pups/litter) at a dose that caused toxicity in parental animals (reduced body wt gain and food consumption) providing qualitative evidence of susceptibility. A DCI for a developmental neurotoxicity study (with extended postnatal treatment) has been issued.

Data Gaps include: Acute Inhalation and 28-Day Inhalation-Rat.

Table 1. Acute Toxicity of Dicrotophos

Guideline No.	Study Type	MRID #(S).	Results	Toxicity Category
81-1	Acute Oral	00261098 /43893901	M/F LD_{50} = 11/8 mg/kg	I
81-2	Acute Dermal	00261098	M/F LD_{50} 876/476 = mg/kg	II
81-4	Primary Eye Irritation	00261098	Lesions reversed by 14 days	II
81-5	Primary Skin Irritation	00261098	No irritation	IV
81-6	Dermal Sensitization	00261098	Strong sensitizer	-

3.2 FQPA Considerations

Based on newly submitted studies and reevaluation of existing studies, the FQPA Safety Factor Committee recommended that the FQPA safety factor for dicrotophos be reduced to 3x for all population subgroups when assessing chronic dietary exposure only(HED DOC NO 014699, B. Tarplee). This supercedes the previous recommendation from the FQPA Recommendations for the Organophosphates that 10x be retained for acute and chronic endpoints. The FQPA committee recommended that the safety factor be reduced to 3x for all population subgroups when assessing chronic dietary exposure because there is qualitative evidence of increased susceptibility in the multigeneration reproduction study but there is no quantitative or qualitative evidence of increased susceptibility following *in utero* exposure to dicrotophos in the prenatal developmental studies in rats or rabbits. The 3x safety factor is required only for chronic dietary exposure since concern for susceptibility seen in the multigeneration reproduction study is not considered to result from an acute exposure.

3.3 Dose Response Assessment

Table 2. Doses and Toxicological Endpoints for Various Exposure Scenarios

EXPOSURE SCENARIO	DOSE	ENDPOINT	STUDY
Acute Dietary	LOAEL= 0.5 mg/kg/day UF = 300 FQPA=1	The value of 0.5 mg/kg was recommended for the endpoint because at this level plasma, RBC and brain ChE on day 1 was observed (a NOAEL was not established).	Acute Neurotoxicity -Rat
	FQPA = 1 Acute RfD = 0.0017 mg/kg Acute PAD = 0.0017		
Chronic Dietary	LOAEL= 0.02 mg/kg/day UF = 300 FQPA=3	The value of 0.02 mg/kg was recommended for the endpoint because at this level plasma, RBC and brain ChE in both sexes was observed (a NOAEL was not established).	Chronic Toxicity -Rat
	FQPA = 3 Chronic RfD = 0.00007 mg/kg/day Chronic PAD = 0.00002 mg/kg/day		
Short-Term (Dermal)	LOAEL= 2.0 mg/kg/day MOE=300[a]	Decreased RBC ChE activity in male rats and decreased plasma ChE activity in female rats (a NOAEL was not established).	28 Day Dermal Toxicity-Rat[b]
Intermediate-Term (Dermal)	LOAEL= 2.0 mg/kg/day MOE=300	Decreased RBC ChE activity in male rats and decreased plasma ChE activity in female rats (a NOAEL was not established).	28 Day Dermal Toxicity-Rat
Long-Term (Dermal)	LOAEL= 2.0 mg/kg/day MOE=300	Decreased RBC ChE activity in male rats and decreased plasma ChE activity in female rats (a NOAEL was not established).	28 Day Dermal Toxicity-Rat
Inhalation[c] Short- Intermediate- Long-	LOAEL= 0.5 mg/kg/day 0.04 mg/kg/day 0.02 mg/kg/day UF = 300	The values were recommended for the endpoint because at this level plasma, RBC and/or brain Che was observed (a NOAEL was not established).	Acute Neurotoxicity - Rat; Subchronic Neurotoxicity-Rat; Chronic Toxicity-Rat

[a] An MOE of 300 applies to occupational exposure/risk assessment.

[b] 21 day treatment with 1 week follow-up period without treatment

[c] 100% inhalation absorption rate should be used for risk assessment

3.3.1 Dietary Endpoints

3.3.1.1 Acute Reference Dose (RfD)

A rat acute neurotoxicity resulted in an LOAEL of 0.5 mg/kg based on the plasma, RBC or brain ChE observed on Day 1 (a NOAEL was not established). This dose is appropriate since the effects were observed on Day 1 following a single dose. Also, an additional Uncertainty Factor (UF) of 3 was applied for the use of a LOAEL for risk assessment. Uncertainty Factor (UF): 300 (10 x for inter-species extrapolation, 10 x for intra-species variability and 3 x for lack of a NOAEL).

Acute RfD = $\frac{0.5 \text{ mg/kg}}{300 \text{ (UF)}}$ = **0.0017 mg/kg.** **Acute PAD** = $\frac{\text{RfD}}{1 \text{ (FQPA SF)}}$ = **0.0017 mg/kg**

3.3.1.2 Chronic RfD

A rat combined chronic toxicity carcinogenicity resulted in an LOAEL of 0.02 mg/kg based on was recommended for the endpoint because at this level the plasma, RBC or brain ChE in both sexes was observed (a NOAEL was not established). An additional Uncertainty Factor of 3 was applied for the use of a LOAEL for risk assessment. Uncertainty Factor (UF): 300 (10 x for inter-species extrapolation, 10 x for intra-species variability and 3 x for lack of a NOAEL).

Chronic RfD = $\frac{0.02 \text{ mg/kg/day}}{300 \text{ (UF)}}$ = **0.00007 mg/kg/day** **Chronic PAD** = $\frac{\text{RfD}}{3 \text{ (FQPA SF)}}$ = **0.00002mg/kg**

3.3.2 Occupational/Residential Exposure Endpoints

There are no residential uses. Therefore, doses and toxicology endpoints were selected only for occupational exposure risk assessments.

3.3.2.1 Dermal Absorption

Dermal Absorption Factor: For the April 5, 2000 dicrotophos risk assessment, a dermal absorption factor of 15% from a well-conducted, acceptable guideline dermal absorption study for monocrotophos was used in conjunction with an oral LOAEL to assess short and intermediate-term dermal exposure. The registrant has since submitted a dermal absorption study conducted with dicrotophos (MRID 4599501). The new study is a well-conducted, acceptable guideline dermal absorption study. This study indicates a higher dermal absorption of 28% based on potential 10 hour exposure at the low dose level of 0.04 mg/cm^2. However, new route-specific dermal endpoints have been selected based on newly submitted dermal toxicity studies. Therefore, a dermal absorption factor is no longer required for the risk assessment.

3.3.2.2 Dermal Exposure (Any Time Period)

For the previous risk assessment, an acute oral rat neurotoxicity study was used to select an endpoint for short-term dermal exposure and a subacute oral rat oral neurotoxicity study was used to select endpoints for intermediate and long-term dermal exposures. However, an acceptable/guideline route-specific dermal study which measures the effects of concern is now available. The 21/28-Day rat dermal toxicity study establishes a LOAEL of 2 mg/kg/day based on decreased erythrocyte ChE activity in male rats and decreased plasma ChE activity in female rats. An additional 3x factor is applied for use of a LOAEL. The target MOE is 300 for the dermal exposure assessment (10 x for inter-species extrapolation, 10 x for intra-species variability and 3x for lack of a NOAEL). The rat dermal toxicity LOAEL of 2 mg/kg/day is considered an appropriate endpoint for all dermal exposure scenarios (short and intermediate-term) because the ChE inhibition was observed following treatment for 21 days where a steady state was achieved over the 28 day duration treatment.

3.3.2.3 Inhalation Exposure (Any Time Period).

Due to the lack of an acceptable inhalation study, oral LOAELs were selected as the appropriate endpoints. One hundred percent absorption was assumed. The target MOE is 300 for the inhalation exposure assessment (10 x for inter-species extrapolation, 10 x for intra-species variability and 3x for lack of a NOAEL).

3.3.2.4 Carcinogenicity

The CARC determined that dicrotophos was not carcinogenic to male and female CD-1 rats and considered the dosing to be adequate and not excessive in both sexes at 25 ppm based on clinical signs indicative of cholinesterase inhibition and effects on hematological parameters including elevated white blood cell counts (up to 142% of the control value in males and 179% in females) and mild leukocytosis at 25 ppm in both sexes and decreased survival of animals at 50 ppm.

Based on the occurrence of tumors in the mouse study, three members of the Committee considered that the "Data are inadequate for an assessment of human carcinogenic potential" because of a lack of pertinent or useful data or the existing evidence is conflicting (e.g., some evidence is suggestive of carcinogenic effects) but other equally pertinent evidence does not confirm a concern. No new study in mice was requested. However, the majority of the CARC concluded that there is "Suggestive evidence of carcinogenicity, but not sufficient to assess human carcinogenic potential" because the evidence from animal data is suggestive of carcinogenicity, which raises a concern for carcinogenic effects but is judged not sufficient for a conclusion as to human carcinogenic potential. Such evidence includes evidence only in a single study.

3.4 Endocrine Disrupter Effects

EPA is required under the FFDCA, as amended by FQPA, to develop a screening program to determine whether certain substances (including all pesticide active and other ingredients) "may have an

effect in humans that is similar to an effect produced by a naturally occurring estrogen, or other such endocrine effects as the Administrator may designate." Following the recommendations of its Endocrine Disruptor Screening and Testing Advisory Committee (EDSTAC), EPA determined that there was scientific bases for including, as part of the program, the androgen and thyroid hormone systems, in addition to the estrogen hormone system. EPA also adopted EDSTAC's recommendation that the Program include evaluations of potential effects in wildlife. For pesticide chemicals, EPA will use FIFRA and, to the extent that effects in wildlife may help determine whether a substance may have an effect in humans, FFDCA authority to require the wildlife evaluations. As the science develops and resources allow, screening of additional hormone systems may be added to the Endocrine Disruptor Screening Program (EDSP).

When the appropriate screening and/or testing protocols being considered under the Agency's EDSP have been developed, dichrotophos may be subjected to additional screening and/or testing to better characterize effects related to endocrine disruption.

4.0 EXPOSURE ASSESSMENT

4.1 Summary of Registered Uses

Dicrotophos (dimethyl phosphate of 3-hydroxy-N,N-dimethyl-cis-crotonamide) is a contact, systemic acaricide/insecticide registered for use on cotton. The reregistration of dicrotophos is being supported by Amvac Chemical Corporation, the basic producer. Dicrotophos end-use products are marketed in the United States under the trade name Bidrin®; the only dicrotophos end-use formulation currently registered is a water-miscible formulation which may be applied foliarly to established cotton plants.

A specimen label for an 82% a.i. water miscible insecticide formulation of dicrotophos (Product name = Bidrin® 8, EPA Reg. No. 352-466, 2.0 lbs ai/qt) permits the use on cotton for the control of aphids, thrips, spider mites, cotton fleahoppers, grasshoppers, boll weevils, stinkbugs, black fleahoppers, plant bugs (lygus), saltmarsh caterpillars, and leaf perforators. Described below is the proposed use pattern.

Label directions for dicrotophos permit early season, ground application at a maximal rate of 0.2 lb ai/A/application. For mid and late season applications, a maximum application rate of 0.5 lb ai/A/application is permitted. Application may be repeated, up to a total of 3 times per season. Application of this product through irrigation systems is prohibited. There is a general 30 day PHI for harvest. Grazing of livestock is prohibited.

4.2 Dietary Exposure

4.2.1 Food Sources

Tolerances are currently established and expressed in terms of dicrotophos (Dimethyl phosphate of 3-hydroxy-N,N-dimethyl-cis crotonamide) in or on the raw agricultural commodities **cottonseed** (0.05 ppm) and pecans (0.05 ppm) [40 CFR §180.299]. The tolerance expression and dietary risk assessment for dicrotophos should be expressed in terms of the combined residues of dicrotophos and its metabolite monocrotophos (calculated as dicrotophos).

4.2.1.1 Nature of the Residue in Plants and Animals

The nature of the residue in livestock and poultry is adequately understood. Animal metabolism studies were conducted in poultry and ruminants. The majority of ^{14}C-residues (78-100%) in the goat were characterized or identified. Neither dicrotophos or monocrotophos were detected in eggs and poultry tissues, or milk and ruminant tissues. The metabolites found in animals are structurally similar to those found in cotton. HED concluded that tolerances are not required for livestock commodities. The nature of the residue in cotton is adequately understood. The residues of concern are dicrotophos and monocrotophos.

4.2.1.2 Residue Analytical Methods

The recommended change in tolerance expression requires that an appropriate enforcement method be available to determine all dicrotophos residues of concern in/on plant commodities. For the purpose of reregistration, adequate methods are available for the enforcement of plant commodity tolerances. Analytical methods for determination of dicrotophos residues of concern in animal commodities are not needed because tolerances are not needed for eggs, milk, and edible livestock tissues. The Pesticide Analytical Manual (PAM) Volume II (Section 180.299) lists two GLC methods (designated as Methods A and B) with KCl thermionic detection. Both of these methods detect residues of dicrotophos and monocrotophos, but not other cholinesterase-inhibiting metabolites. A later method used for the field trials has completed a successful independent laboratory validation and Agency validation is pending.

4.2.1.3Multiresidue Methods

The reregistration requirements for multiresidue method testing are fulfilled. The 2/97 FDA PESTDATA database (PAM Volume I, Appendix I) indicates that dicrotophos is completely recovered (>80%) using Multiresidue Methods Section 302 (Luke Method; Protocol D) but is not recovered using Multiresidue Methods Section 303 (Mills, Onley, Gaither Method; Protocol E, nonfatty foods).

Monocrotophos is completely recovered (>80%) using Multiresidue Methods Section 302 (Luke Method; Protocol D) but is not recovered using method Sections 303 (Mills, Onley, and Gaither Method; Protocol E for nonfatty food) and 304 (Mills method; Protocol E for fatty food).

4.2.1.4 Storage Stability Data

The reregistration requirements for storage stability data are satisfied. The total storage intervals between harvest and analysis of samples from previously evaluated cotton field and processing studies were ~5 months. Recently submitted storage stability data indicate that fortified residues of dicrotophos and monocrotophos are stable during frozen storage (<-20 ±5 C) for at least 6 months in/on undelinted cottonseed, cotton gin trash, and cottonseed processed commodities. These storage stability data are adequate to support the storage intervals and conditions of samples collected from the cottonseed field and processing studies.

4.2.1.5 Crop Field Trials

The submitted field trial data of dicrotophos residues in/on cottonseed and cotton gin byproducts are adequate. Treatment of crops and timing of applications adequately reflected label directions. Applications were made using ground equipment, with application volume of 14.9 to 20.9 gallons per acre. Application rates ranged from 0.24-0.26 lb ai/A (~1x the maximum label rate) for the early season application and from 0.48-0.53 lb ai/A (~1x the maximum label rate) for the mid and late season application. No unusual or adverse conditions existed following application of dicrotophos. Time from treatment to sampling ranged from 28 to 36 days (PHI).

For undelinted cottonseed, combined residues of dicrotophos and monocrotophos ranged from <0.02 ppm (non-detectable) to 0.13 ppm. Based on the existing dicrotophos and monocrotophos residues from the cotton field trials, the existing dicrotophos tolerance of 0.05 ppm is too low. The recommended tolerance for combined dicrotophos regulated residues (dicrotophos and monocrotophos) in/on cottonseed is 0.2 ppm. For cotton gin byproducts, combined residues of dicrotophos and monocrotophos ranged from 0.12 ppm to 1.8 ppm. There is no existing tolerance established for dicrotophos in/on cotton gin byproducts. HED recommends that the tolerance for regulated residues of dicrotophos in/on cotton gin byproducts be established at 2.0 ppm.

4.2.1.6 Processed Food/Feed

HED has evaluated residue data pertaining to the potential for concentration of dicrotophos residues of concern in the processed commodities of cotton. The cotton processing data indicate that dicrotophos and monocrotophos residues did not concentrate in hulls, meal, and refined oil processed from cottonseed bearing detectable dicrotophos residues and nondetectable monocrotophos residues. Tolerances are, therefore, not required for the processed commodities of cotton.

4.2.1.7 Meat, Milk, Poultry, Eggs

The reregistration requirements for studies pertaining to magnitude of the residue in milk, eggs, and tissues of animals are waived. Based on the results of dicrotophos animal metabolism studies, there is no reasonable expectation of residues in milk, eggs, and tissues of animals [Category 3 of 40 CFR §180.6(a)] when dicrotophos is applied according to registered use directions. Therefore, tolerances for residues of dicrotophos in animal commodities need not be proposed.

4.2.1.8 Confined Accumulation in Rotational Crops

The reregistration requirements for confined/field rotational crop studies are fulfilled. The available confined rotational crop data indicate that the metabolism of dicrotophos in rotational crops is similar to that in primary plants. Because no residues of dicrotophos or monocrotophos were detected in any rotational crop commodity at any plant back interval, no field rotational crop studies are required. In addition, no rotational crop tolerances or restrictions need be established.

4.2.1.9 CODEX Harmonization

The Codex Alimentarius Commission has not established or proposed maximum residue limits (MRLs) for residues of dicrotophos. Therefore, there are no issues regarding compatibility of U.S. tolerances with Codex MRLs.

4.2.2 Drinking Water Sources

4.2.2.1 Surface Water Estimates

Estimates of environmental concentrations of dichrotophos in surface water sources of drinking water have been updated for this assessment. Using the Index Reservoir (IR) and Percent Crop Area (PCA) modifications to the PRZM-EXAMS model and available environmental fate data for parent dicrotophos, EFED calculated the following Tier 2 Estimated Environmental Concentrations (EECs) for residues of dicrotophos in surface water: acute or peak EECs of 2.56 ppb and Chronic (one in 10 year upper 10^{th} percentile) EECs of 0.23 ppb.

The major route of dissipation for dicrotophos in the environment is microbial-mediated degradation in soil. Dicrotophos may also move into surface water through runoff if sufficient rainfall occurs close to the time of application.

The USGS Organic Geochemistry Research Group conducted a regional surface water study in the Mississippi Embayment in 1996 and 1997 in which dicrotophos was detected. A total of 162 samples were collected from 64 locations on rivers within the cotton-growing regions of Missouri, Kentucky, Arkansas, Tennessee, Mississippi, and Louisiana, and analyzed for the presence of cotton pesticides. Samples were intended to represent ambient conditions. Dicrotophos was the most frequently detected insecticide being found above detection limits in 45 samples (28%). Six samples had dicrotophos concentrations above 0.5 ppb. The maximum concentration detected was 4.99 ppb. Although most residents of the cotton growing areas in the Mississippi Embayment apparently obtain their drinking water from groundwater sources, there are a few public (surface) water supplies in the region). Therefore, EFED cannot rule out the possibility of drinking water exposures at the calculated EECs recommended in this document.

Laboratory studies showed that abiotic hydrolysis rates were pH-dependent (alkaline-catalyzed), and followed first-order kinetics. The calculated half-lives for dicrotophos in sterile aqueous solutions at pH 5, 7, and 9 were 117, 72, and 28 days, respectively. The estimated half-life values at pH 5 and 7 exceed the length of the study (28 days). The calculated half-life for the aqueous photolysis study was

48 days at pH 7. In the soil surface photolysis study, 80% of the applied parent was recovered in both the light and dark controls after 30 days of exposure. Laboratory soil metabolism studies showed that dicrotophos degraded rapidly under aerobic and anaerobic conditions. Under aerobic conditions, the soil half-life of dicrotophos was 2.7 days in a Hanford sandy loam soil (pH 5.7). Under anaerobic conditions, dicrotophos degraded with a half-life of 7 days in a Hanford sandy loam soil. Supplemental soil TLC studies showed that aged dicrotophos was highly mobile in sandy soil and of intermediate mobility in sandy loam soil. In supplemental terrestrial field studies in Mississippi and Georgia, dicrotophos dissipated with a half-life of 2.2 days. The registrant reported the vapor pressure of dicrotophos as 2.9 mPa at 20°C, which is equivalent to 2.2×10^{-5} mm Hg at 20°C. A laboratory volatility study on soil, using the technical ingredient, showed that only 0.1% of applied dicrotophos volatilized after 7 days.

4.2.2.2 Groundwater Estimates

Using the SCI-GROW model described below, EFED calculated an EEC of 0.005 ppb for dicrotophos in ground water.

4.2.2.3 Drinking Water Model Characterization

Surface Water: EFED conducted a revised surface water analysis used the PRZM/EXAMS model with Index Reservoir and Percent Crop Area modifications to calculate Tier II refined EECs. The Pesticide Root Zone Model(PRZM 3.1) simulates pesticides in field runoff, while the Exposure Analysis Modeling System (EXAMS, version 2.97-5) simulates pesticide fate and transport in an aquatic environment. The Index Reservoir replaces the standard pond (one hectare body of water, two meters deep) in PRZM/EXAMS. The Index Reservoir is modeled as a continuous-flow stirred tank-reactor with a flow rate set to reflect run-off derived from local weather conditions and soils associated with a watershed representative of a particular crop. The PRZM/EXAMs output for the Index Reservoir is then multiplied by the PCA, which is the estimated maximum percent of agricultural land within any watershed that is planted to that crop. For cotton, the PCA is 20%.

Ground Water: Ground water calculations for parent dicrotophos were based on the SCI-GROW model (Screening Concentrations in Ground Water), which is a model for estimating concentrations of pesticides in ground water under "worst case" conditions. SCI-GROW provides a screening concentration or an estimate of likely ground water concentration if the pesticide is used at the maximum allowed label rate in areas with ground water that is exceptionally vulnerable to contamination. In most cases, a majority of the use area will have ground water that is less vulnerable to contamination than the areas used to derive the SCI-GROW estimate. The SCI-GROW model is based on normalized ground water concentrations from ground water monitoring studies, environmental fate properties (aerobic soil half-lives and organic carbon partitioning coefficients - K_{oc}'s) and application rates. The model is based on permeable soils that are vulnerable to leaching and that overlay shallow ground water (10-30 feet).

4.2.3 Food Source Risk Assessment And Characterization

4.2.3.1 Chronic Dietary Exposure

A revised chronic dietary exposure analysis was conducted using the DEEM™ software and a revised chronic dietary endpoint (D278883 B.Daiss 10/30/01). This analysis is based on consumption data obtained from respondents in the USDA 1989-91 Continuing Surveys for Food Intake by Individuals (CFSII). Cottonseed residue data from crop field trials were averaged resulting in 0.04 ppm. The estimated average percent crop treated data provided by BEAD of 8% was included in the calculation by using a second adjustment factor in DEEM. The resulting exposure for the general US population was <0.000001 mg/kg/day. The percent of cPAD occupied is provided for the US population and most highly exposed subpopulation, children 1-6 years of age, in Table 3.

Table 3. Chronic Dietary (Food) Exposure Estimate and Percent of Acute RfD Occupied (Tier 3 Exposure Analysis using 11% crop treated and avg. field trial residues).

Population Subgroup	Chronic Dietary (Food) Exposure (mg/kg/day)	Percent of Chronic PAD
U.S. Population	<0.000001	0.1
Children 1-6 years old	<0.000001	0.9

4.2.3.2 Acute Dietary Exposure

A revised acute dietary exposure analysis was conducted for dicrotophos using the DEEM™ software and the new acute dietary endpoint. This analysis is based on consumption data obtained from respondents in the USDA 1989-91 Continuing Surveys for Food Intake by Individuals (CFSII). Since the only commodity with registered use of dicrotophos (cotton) is considered to be blended, residues from crop field trials were averaged resulting in 0.04 ppm. The estimated maximum percent crop treated data provided by BEAD of 11% was included in the calculation by using a second adjustment factor in DEEM™. The percent of aPAD occupied and level of exposure for the US population and the most highly exposed subpopulation, children 1-6 years of age, are provided in Table 4.

Table 4. Acute Dietary (Food) Exposure Estimate and Percent of Acute RfD Occupied at the 99.9th Percentile (Tier 3 Exposure Analysis Using 11% crop treated and avg. field trial residues).

Population Subgroup	Acute Dietary Exposure (mg/kg/day)	Percent aPAD
US Population	0.000002	0.12
Children 1-6 years old	0.000004	0.27

4.2.4 Drinking Water Risk Assessment and Characterization

Based on the chronic and acute dietary exposure estimates presented in Tables 4 and 5, drinking water levels of comparison (DWLOC) were re-calculated using the formulas presented below. A

DWLOC is the concentration of a pesticide in drinking water which would result in an unacceptable risk, after factoring in all food and other non-occupational exposures for which OPP has reliable data.

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

$$\mathbf{DWLOC_{acute}}\text{ children 1-6} = \frac{0.00166 \times 10}{1 \times 0.001} = 17\text{ ppb}$$

where acute water exposure (mg/kg/day) = [aPAD (0.0002mg/kg/day)- (acute food exposure) (mg/kg/day)]
(i.e. 0.00166mg/kg/day - 0.000004mg/kg/day = 0.00166 mg/kg/day)

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

$$\mathbf{DWLOC_{chroni}}\text{ children 1-6} = \frac{0.00002 \times 10}{1 \times 0.001} = 0.2\text{ ppb}$$

where chronic water exposure (mg/kg/day) = [cPAD (0.000007 mg/kg/day)- (chronic food exposure) (mg/kg/day)]
(i.e. 0.00002 mg/kg/day - 0.0000002 mg/kg/day = 0.00002 mg/kg/day)

The Agency's default body weights and consumption values used to calculate DWLOCs are as follows: 70 kg/2L/day (adult male), 60 kg/2L/day (adult female) and 10 kg/1L/day (child).

4.2.4.1 Acute DWLOC

Based on the above-calculated acute exposure from food, HED calculated the acute Drinking Water Level of Comparison ($DWLOC_{acute}$) for acute exposures to dicrotophos. The DWLOC is the concentration in drinking water which, when combined or aggregated with exposures through food, would result in an aggregate exposure which is just acceptable. In other words, it is the theoretical concentration of a pesticide in drinking water which would be an acceptable upper limit in light of the total aggregate exposure to that pesticide through all pathways. If model-based estimated concentrations in ground and surface waters are less than the $DWLOC_{acute}$, OPP can conclude with reasonable certainty that aggregate exposures through food and drinking water do not exceed HED's level of concern.

HED's calculated $DWLOC_{acute}$ is 17 ppb (based on the most highly exposed subgroup, children 1-6). Environmental Fate and Effects Division's (EFED's) model-based estimates for maximum concentrations in surface and ground water are 2.6 ppb and 0.005 ppb, respectively. Since the model-based estimate for concentrations in surface water (2.6 ppb) and groundwater (0.005) are below HED $DWLOC_{acute}$ of 17 ppb HED concludes that with reasonable certainty that aggregate exposure to dicrotophos through food and surface water and food and ground water will not result in unacceptable exposure and risk.

4.2.4.2 Chronic DWLOC

Based on the above-calculated chronic exposure from food, HED has also calculated the chronic Drinking Water Level of Comparison ($DWLOC_{chronic}$) for chronic exposures to dicrotophos. HED's calculated $DWLOC_{chronic}$ is 0.22 ppb (based on the most exposed subgroup, children 1-6). EFED's model-based estimates for average concentrations of dicrotophos in surface and ground water are 0.23 ppb and 0.005 ppb, respectively. Since the model-based estimate for concentrations in surface water (0.23 ppb) is essentially equal to HED's $DWLOC_{chronic}$ of 0.22 ppb, and both the dietary exposure

estimate and the EEC were calculated using reasonably conservative assumptions, HED concludes with reasonable certainty that aggregate exposure to dicrotophos through food and surface water will not result in unacceptable exposure and risk. Model estimates for dicrotophos in ground water are below $DWLOC_{chronic}$, therefore, aggregate exposure to dicrotophos through food and ground water will not result in unacceptable exposure and risk.

4.3 Occupational Exposure and Risk

At this time products containing dicrotophos are intended for occupational use only. It is classified as Restricted Use and may be purchased and used only by certified applicators or persons under their direct supervision. Dicrotophos (3-hydroxy-N, N-dimethyl-cis-crotonamide, dimethyl phosphate) is a contact and systemic organophosphate insecticide. It is formulated as a:

- technical product with 85 percent active ingredient,
- liquid (isopropyl alcohol based) formulation with 82 percent active ingredient (EPA Reg. No. 5481-448).

Currently, dicrotophos is registered for occupational-use on cotton (application rates range from 0.1 to 0.5 pounds active ingredient per acre). Dicrotophos is applied during early, middle, and late season to cotton using aerial or groundboom equipment.

4.3.1 Handler

4.3.1.1 Handler Exposures & Risks

EPA has determined that there are potential exposures to mixers, loaders, applicators, or other handlers during usual use-patterns associated with dicrotophos. Based on the use patterns, 5 major exposure scenarios (each assessed at 3 different application rates) were identified for dicrotophos:

- (1a) mixing/loading liquid formulation to support aerial applications,
- (1b) mixing/loading liquid formulation to support groundboom applications,
- (2) applying spray with aircraft,
- (3) applying spray with groundboom equipment, and
- (4) flagging for aerial spray applications.

4.3.1.2 Handler Exposure Scenarios -- Data and Assumptions

It is the policy of the HED to use data from the Pesticide Handlers Exposure Database (PHED) Version 1.1 to assess handler exposures for regulatory actions when chemical-specific monitoring data are not available. PHED was designed by a task force of representatives from the U.S. EPA, Health Canada, the California Department of Pesticide regulation, and member companies of the American Crop Protection Association. PHED is a software system consisting of two parts -- a database of measured exposure values for workers involved in the handling of pesticides under actual field conditions and a set of computer algorithms used to subset and statistically summarize the selected data. Currently, the database contains values for over 1,700 monitored individuals (i.e., replicates).

Users select criteria to subset the PHED database to reflect the exposure scenario being evaluated. The subsetting algorithms in PHED are based on the central assumption that the magnitude of handler exposures to pesticides are primarily a function of activity (e.g., mixing/loading, applying), formulation type (e.g., wettable powders, granular), application method (e.g., aerial, groundboom), and clothing scenarios (e.g., gloves, double layer clothing).

Once the data for a given exposure scenario have been selected, the data are normalized (i.e., divided by) by the amount of pesticide handled resulting in standard unit exposures (milligrams of exposure per pound of active ingredient handled). Following normalization, the data are statistically summarized. The distribution of exposure values for each body part (e.g., chest upper arm) is categorized as normal, lognormal, or "other" (i.e., neither normal nor lognormal). A central tendency value is then selected from the distribution of the exposure values for each body part. These values are the arithmetic mean for normal distributions, the geometric mean for lognormal distributions, and the median for all "other" distributions. Once selected, the central tendency values for each body part are composited into a "best fit" exposure value representing the entire body.

The unit exposures calculated by PHED generally range from the geometric mean to the median of the selected data set. To add consistency and quality control to the values produced from this system, the PHED Task Force has evaluated all data within the system and has developed a set of grading criteria to characterize the quality of the original study data. The assessment of data quality is based on the number of observations and the available quality control data. These evaluation criteria and the caveats specific to each exposure scenario are summarized in Table 5 (attached pg 29). 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.

A dicrotophos handler exposure study was submitted to PHED (i.e., Bidrin Field Exposure Study in Post-Emergent Application on Cotton, April 7, Shell Oil Co.). The Bidrin study contains applicator replicates for pilots in enclosed cockpits, mixer/loader/applicator replicates using open mixing/loading and enclosed cab groundboom tractors, mixer/loader/applicator replicates using open mixing/loading and open cab groundboom tractors, and open mixing/loading liquid replicates. Both dermal and inhalation exposures were monitored. The data in the study for enclosed cockpit and enclosed cab and groundboom tractor were in the upper percentiles compared to that of the other data available in PHED. A more detailed description and specific results of the study are presented in the Revised Agricultural and Occupational Exposure Assessment Document (D241596, T. Leighton, 10/26/01). According to HED's Science Advisory Council for Exposure Policy 7, "Use of Values from the PHED Surrogate Table and Chemical-Specific Data" (January, 1999), the dicrotophos-specific handler data were combined with other data from the PHED Version 1.1 to assess handler exposures for dicrotophos.

4.3.1.3 Assumptions Used in Handler Exposure Calculations

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

- Average body weight of an adult handler is 70 kg.
- Average work day interval represents an 8 hour workday (e.g., the acres treated or volume of spray solution prepared in a typical day).
- Daily acres to be treated in each scenario include:
  - -- Aerial applications, including flaggers: 350 and 1,200 acres per day as a range-finder, since cotton is typically cultivated on large acreages, and
  - -- Groundboom applications: 80 acres per day.
- Calculations are completed at the application rates for early- and late-season cotton applications as specified by the dicrotophos label to bracket risk levels associated with the various application rates. No use-data were provided by the registrant concerning the actual "typical" application rates that are commonly used for dicrotophos.

4.3.1.4 Handler Exposure and Risk Estimates

Usually handler exposure assessments are completed by EPA using a baseline exposure scenario and, if required, increasing levels of risk mitigation (Personal Protective Equipment (PPE) and engineering controls) are included to achieve an appropriate margin of exposure or cancer risk. The baseline scenario generally represents a handler wearing long pants, a long-sleeved shirt, and no chemical-resistant gloves. If the levels of concern are exceeded at baseline protection, then risks are calculated using personal protective equipment to mitigate exposure. PPE may consist of chemical-resistant gloves, double-layer body protection and/or an appropriate respirator. If the levels of concern are exceeded at PPE level of protection, risks are calculated using engineering controls (if feasible) to mitigate exposure. The occupation exposure and risk calculations are summarized in the attached tables (pgs 30-34). Table 6 presents calculations for occupational handlers of dicrotophos at baseline attire using short- and intermediate-term endpoints for dermal, inhalation, and total exposures. Table 7 presents calculations for occupational handlers of dicrotophos using the short-term endpoints for dermal, inhalation, and total exposures. Table 8 presents calculations for occupational handlers of dicrotophos using the intermediate-term endpoints for dermal, inhalation, and total exposures. Risks are assessed for dermal exposures and inhalation exposures and, since the endpoint of concern is cholinesterase inhibition for both the dermal and inhalation routes (an oral endpoint is used as a surrogate for both), risks are also assessed for combined total exposures. In lieu of route-specific data, an oral LOAEL was selected as the short- and intermediate-term endpoints for occupational inhalation exposures and 100 percent inhalation absorption is assumed.

Potential daily inhalation exposure was calculated using the following formula:

$$\textit{Daily Inhalation Exposure}\left(\frac{mg\ ai}{day}\right) = \textit{Unit Exposure}\left(\frac{\mu g\ ai}{lb\ ai}\right) \times \textit{Conversion Factor}\left(\frac{1mg}{1{,}000\ \mu g}\right) \times \textit{Use Rate}\left(\frac{lb\ ai}{A}\right) \times \textit{Daily Acres Treated}\left(\frac{A}{day}\right)$$

Potential daily dermal exposure was calculated using the following formula:

$$Daily\ Dermal\ Exposure\left(\frac{mg\ ai}{day}\right) = Unit\ Exposure\left(\frac{mg\ ai}{lb\ ai}\right) x\ Use\ Rate\left(\frac{lb\ ai}{A}\right) x\ Daily\ Acres\ Treated\left(\frac{A}{day}\right)$$

The daily dermal and inhalation doses and total doses were calculated using a 70 kg body weight using the following formulas:

$$Daily\ Inhalation\ Dose\left(\frac{mg\ ai}{kg/day}\right) = Daily\ Inhalation\ Exposure\left(\frac{mg\ ai}{day}\right) x\left(\frac{1}{Body\ Weight\ (kg)}\right)$$

100 percent inhalation absorption was assumed in this calculation.

$$Daily\ Dermal\ Dose\left(\frac{mg\ ai}{Kg/Day}\right) = Daily\ Dermal\ Exposure\left(\frac{mg\ ai}{Day}\right) x\left(\frac{1}{Body\ Weight\ (Kg)}\right) x\ Dermal\ Absorption\ Factor\ (0.15)$$

Dermal absorption is not a factor since the dermal endpoint was derived from a dermal study.

Handler exposure assessments were completed using baseline, personal protective equipment, and engineering exposure scenarios. The short- and intermediate-term risks for dermal, inhalation, and total exposures are calculated as follows:

$$MOE = \frac{LOAEL}{DailyDose(dermal,inhalation,total)}$$

In addition, since endpoints of concern for dermal and inhalation routes were based on identical adverse effects (i.e., cholinesterase inhibition) the risks are aggregated. The uncertainty factor for both dermal and inhalation risk is 300. The total risk is calculated as follows:

$$\text{Total } MOE = \frac{1}{\frac{1}{dermal\ MOE} + \frac{1}{inhalation\ MOE}}$$

4.3.1.5 Summary of Risk Concerns for Handlers

Tables 6, 7, and 8 (attached) present estimates of occupational dermal, inhalation, and total risks from handling dicrotophos at baseline, PPE, and when engineering controls are used. An MOE of 300 for both the dermal and inhalation routes is considered adequate for the handler risk assessment. Results from these tables are summarized below.

Dermal

Short- and intermediate term dermal risk: using the short-term dermal endpoint, MOEs for all but two scenarios are less than the target MOE of 300 at baseline. The two exceptions are applying with groundboom equipment and flagging to support aerial spray applications. With PPE, all but the same two scenarios result in MOEs lower than the target MOE of 300. With engineering control mitigation, MOEs are greater than 300 for 4 scenarios. The scenarios greater than 300 include those that exceeded 300 at baseline and/or personal protective equipment protection plus flagging to support aerial applications and mixing/loading to support groundboom applications.

Inhalation

Short-term Inhalation Risk - Using the short-term inhalation end-point, all but two MOEs are greater than the target MOE of 300 at baseline protection. The two exceptions are mixing/loading to support aerial applications at all rates, and applying liquid formulation at the maximum rate for aerial applications. With PPE, MOEs are greater than the target MOE of 300 for all but the mixing/loading to support aerial applications at the highest rate. All MOEs are greater than the target MOE of 300 with engineering control protection.

Intermediate-term Inhalation Risk - Using the intermediate-term inhalation endpoint, all but two MOEs are less than the target MOE of 300 at baseline protection. With PPE, MOEs are greater than the target MOE of 300 for five scenarios. These include mixing/loading to support groundboom applications at the lowest rate, applying with groundboom equipment at the two lowest rates, and flagging to support aerial spray applications at the two lowest rates. Ten MOEs are greater than the target MOE of 300 with engineering control protection. The engineering control scenarios with MOEs below the target MOE of 300 are mixing/loading to support aerial applications at all application rates and applying aerially at the two highest application rates.

Total

Short-term Total Risk - When combining the short-term dermal risks with the inhalation risks, MOEs are greater than the target MOE of 300 for 2 of the baseline scenarios; applying with groundboom equipment and flagging to support aerial spray applications. With PPE, two additional scenarios have MOEs greater than the target MOE of 300; mixing/loading to support groundboom equipment and applying groundboom equipment. At engineering controls, three additional scenarios have MOEs greater than the target MOE of 300; two flagging to support aerial applications and a mixing/loading to support groundboom application. All the remaining short-term MOEs are below 300 even with engineering control protection.

Intermediate-term Total Risk - Results of the intermediate-term handler aggregate assessment indicate that, at baseline, no scenarios have MOEs greater than the target MOE of 300. With PPE, two scenarios have MOEs greater than the target MOE of 300; applying with groundboom equipment, and flagging to support aerial spray applications. With engineering controls mitigation, five additional scenarios have MOEs greater than the target MOE of 300. These are mixing/loading to support groundboom equipment, applying with groundboom equipment, and flagging to support aerial

applications. All the remaining intermediate-term MOEs are below the target MOE of 300 even with engineering control protection.

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

- All handler assessments were completed using PHED data that range from low to high quality. All PHED data for the engineering control scenarios range from medium to high quality;

- Generic protection factors were used to calculate double-layer body protection and a dust/mist respirator for the personal protective equipment scenarios.

- Exposure Factors: In the dermal exposure estimates, the ratio of the body surface area to the body weight overestimates the dose by a factor of 1.1. In addition, HED has agreed to use the NAFTA recommended values for breathing rates rather than the existing rate in Series 875 Group A which recommends an inhalation rate of 29 L/min. The new NAFTA recommended inhalation rates are 8.3, 16.7, and 26.7 L/min for sedentary, light, and moderate activities respectively. These respective inhalation reduction factors 3.5, 1.7, and 1.1. Applying these reduction factors, only two of the total MOEs that are below the target MOE of 300 would be elevated above 300. (i.e., short-term total MOE for the groundboom applicator at the maximum rate and the intermediate-term total MOE for the mixer/loader for the groundboom applicator at the 0.2 lb ai/acre rate).

4.3.2 Postapplication

4.3.2.1 Postapplication Exposure Scenarios

HED has determined that there are potential postapplication exposures to:

- workers entering treated cotton fields to perform irrigating and hand weeding tasks during the early and late season,
- workers entering treated cotton fields to perform hand harvesting tasks,
- workers entering treated cotton fields to perform mechanical harvesting tasks, and
- handlers entering treated cotton fields to perform scouting and crop-advising tasks during the early season and late season.

Postapplication risks are mitigated for crop advisors/scouts using entry restrictions, not restricted-entry intervals. Since, under the Worker Protection Standard for Agricultural Pesticides (40 CFR Part 170), crop advisors/scouts are defined as handlers, the Agency can permit such persons to enter treated areas to perform scouting tasks, provided they are using required personal protective equipment. Postapplication requirements for crop advisors/scouts for dicrotophos are based on the individual and averaged residue measurements from a dislodgeable foliar residue (DFR) study conducted in two geographical areas (Texas, and Mississippi) (see attached Tables 9, 10, and 11).

Postapplication risks are mitigated for workers using a restricted-entry interval (REI). In general, the REI is established based on the number of days following application that must elapse before the pesticide residues dissipate to a level where estimated worker MOE's equal or exceed 300 while wearing baseline attire (i.e., long-sleeve shirt, long pants, shoes, and socks). Under the Worker Protection Standard for Agricultural Pesticides (WPS) – 40 CFR Part 170, entry to perform routine hand labor tasks is prohibited during an REI and personal protective equipment cannot be considered as a risk reduction measure in establishing the REI. REI requirements for dicrotophos are based on the individual and averaged residue measurements from a dislodgeable foliar residue (DFR) study conducted in two geographical areas (Texas, and Mississippi) (Tables 9, 10, and 11).

4.3.2.2 Data Source Descriptions for Scenarios Considered

The registrant submitted postapplication dicrotophos exposure data in response to the data requested by the Agency during Phase 4 of the reregistration process. One DFR study was submitted for dicrotophos. The study, titled *Dissipation of Dicrotophos Dislodgeable Foliar Residues on Cotton Treated with Bidrin* (MRID No. 44731001) is summarized in the Revised Agricultural and Occupational Exposure Assessment (D358391, T. Leighton, 10/26/01).

4.3.2.3 Assumptions Used in Postapplication Exposure Calculations

The assumptions used in the calculations for occupational postapplication risks include the following:

- Daily exposure is assumed to occur for 8 hours per day
- The median body weight of 70 kg is used, representing a typical adult.

4.3.2.4 Postapplication Exposure and Risk Estimates

The postapplication risks from dicrotophos has been assessed using dicrotophos-specific regression data and standard values for transfer coefficients.

Daily Absorbed Doses were calculated as follows:

$$Dose\ (mg/kg/day) = \frac{(DFR\ (\mu g/cm^2)\ x\ Tc\ (cm^2/hr)\ x\ CF\left(\frac{1\ mg}{1{,}000\ \mu g}\right)\ x\ ED\ (hrs/day))}{BW}$$

Where:

DFR	=	daily DFR ($\mu g/cm^2$)
Tc	=	transfer coefficient; 4,000 cm^2/hr for late season scouting; and 1,000 cm^2/hr for early season scouting and hoeing
CF	=	conversion factor (i.e., 1 mg/1,000 μg)
ED	=	exposure duration; 8 hours worked per day for scouting and hoeing
BW	=	body weight (70 kg)

Short- and intermediate-term MOEs were calculated as follows:

$$MOE = \frac{LOAEL}{Dose}$$

Where:

LOAEL = 0.5 mg/kg/day[1]
Dose = calculated absorbed dermal dose

Table 9 presents the short- and intermediate-term dermal MOEs for hand harvesting activities. It indicates that for hand harvesting activities, the margin of exposure (MOE) for short- and intermediate-term postapplication exposures exceeds 300 at day 8 using the combined (averaged) DFRs for the two sites.

Table 10 presents the short- and intermediate-term dermal MOEs for the late season activities of scouting, irrigating, and hand weeding. It indicates that for late season activities, the margin of exposure (MOE) for short- and intermediate-term postapplication exposures exceeds 300 at day 6 using the combined (averaged) DFRs for the two sites.

Table 11 presents the short- and intermediate-term dermal MOEs for early season activities of scouting, irrigating, and hand weeding. It indicates that for early season activities, the margin of exposure for short- and intermediate-term postapplication exposures exceeds 300 at day 0 for the combined (averaged) DFRs for the two sites.

4.4 Residential Exposure

There are no registered uses that would result in residential exposure.

5.0 AGGREGATE RISK ASSESSMENTS AND RISK CHARACTERIZATION

Aggregate risk is estimated by combining dietary (food and water) and residential exposures. Dicrotophos has no uses that could result in residential exposure, therefore, the aggregate risk estimate will be based on the dietary exposure from food and water only, for the most highly exposed population subgroups and the general population as appropriate. Details concerning the assumptions used in deriving exposure estimates and risk characterizations were discussed previously in this document.

6.0 CUMULATIVE EXPOSURE AND RISK

The Food Quality Protection Act (1996) stipulates that when determining the safety of a pesticide chemical, EPA shall base its assessment of the risk posed by the chemical on, among other things, available information concerning the cumulative effects to human health that may result from dietary, residential, or other non-occupational exposure to other substances that have a common mechanism of toxicity. The reason for consideration of other substances is due to the possibility that low-level exposures to multiple chemical substances that cause a common toxic effect by a common mechanism could lead to the same adverse health effect as would a higher level of exposure to any of the

other substances individually. A person exposed to a pesticide at a level that is considered safe may in fact experience harm if that person is also exposed to other substances that cause a common toxic effect by a mechanism common with that of the subject pesticide, even if the individual exposure levels to the other substances are also considered safe.

Dicrotophos is a member of the organophosphate (OP) class of pesticides. All pesticides of this class contain phosphorus and other members of this class of pesticides are numerous and include Azinphos Methyl, Chlorpyrifos, Chlorpyrifos-Methyl, Diazinon, Dichlorvos, Dimethoate, Disulfoton, Methamidophos, Methidathion, Monocrotophos, Naled Oxydemeton-Methyl, Phorate, Phosmet, Pirimiphos-Methyl, and Trichlorfon to name a few. EPA considers organophosphates to express toxicity through a common biochemical interaction with cholinesterase which may lead to a myriad of cholinergic effects. Consequently the organophosphate pesticides should be considered as a group when performing cumulative risk assessments.

HED has recently developed guidance for conducting cumulative risk assessments on substances that have a common mechanism of toxicity. This guidance was issued for public comment on June 30, 2000 (65 FR 40644-40650) (http://www.epa.gov/fedrgstr/EPA-PEST/2000/June/Day-30/6049.pdf) and is expected to be finalized in November, 2001. The guidance is currently being used by EPA to conduct a cumulative assessment of the organophosphate pesticides. The OP cumulative assessment is expected to be completed in December, 2001

7.0 DATA NEEDS

Acute Inhalation - GL # 870.1300
28-Day Inhalation-Rat - GL # 870.3465

Agricultural/Occupational Assessment Tables Attached

Table 5. Occupational Exposure Scenario Descriptions for the Use of Dicrotophos

Exposure Scenario (Number)	Data Source	Standard Assumptions[a,b]	Comments[c]
Mixer/Loader Descriptors			
Mixing/Loading Liquid Formulations (1a, 1b)	PHED V1.1	Eight-hour work day; Mixing/loading to support aerial application: 1200 acres per day; Mixing/loading to support groundboom application: 200 acres per day	**Baseline:** Dermal (72 to 122 replicates); hand (53 replicates); and inhalation (85 replicates) exposure values are all based on AB grade data. High confidence in the unit exposure values. No protection factors were needed to define the unit exposure value. **PPE:** The same dermal and inhalation data are used as for the baseline coupled with a 50% protection factor to account for an additional layer of clothing and a 5-fold protection factor to account for the use of a dust/mist respirator. Hand (59 replicates) exposure value is based on AB grade data. High confidence in the unit dermal exposure value. **Engineering Controls:** Dermal (31 replicates) exposure value is based on AB grade data. Hand (31 replicates) and inhalation (27 replicates) exposure values are based on AB grade data. High confidence in the dermal unit exposure value. Low confidence in inhalation unit exposure value. Empirical data include the use of chemical-resistant gloves. No protection factors were needed to define the unit exposure value.
Applicator Descriptors			
Applying Sprays with Aircraft (2)	PHED V1.1	Eight-hour work day and 1200 acres per day	**Baseline and PPE:** These scenarios are not considered an option for this assessment as a vast majority of agricultural aircraft are closed cab vehicles (i.e., the scenario defaults to engineering controls). **Engineering controls:** Dermal (24 to 48 replicates) and inhalation (23 replicates) exposure values are based on ABC grade data. Hand (34 replicates) exposure value is based on AB grade data. Medium confidence in the unit exposure value. No protection factors were needed to define the unit exposure
Applying Sprays with a Groundboom Sprayer (3)	PHED V1.1	Eight-hour work day and 200 acres per day	**Baseline:** Dermal (23 to 42 replicates); hand (29 replicates); and inhalation (22 replicates) exposure values are based on AB grade data. High confidence in the unit exposure values. No protection factors were required to define the unit exposure value. **PPE:** The same dermal and inhalation data are used as for the baseline coupled with a 50% protection factor to account for an additional layer of clothing and a 5-fold protection factor to account for the use of a dust/mist respirator. Hand (21 replicates) exposure value is based on ABC grade data. Medium confidence in the unit exposure values. **Engineering Controls:** Dermal (20 to 31 replicates) and hand (16 replicates) exposure values are based on ABC grade data. Inhalation (16 replicates) exposure value is based on AB grade data. Medium confidence in unit exposure value. No protection factors were required to define the unit exposure value.
Flagger Descriptors			
Flagging Aerial Spray Applications (4)	PHED V1.1	Eight-hour work day and 350 acres per day	**Baseline:** Dermal (18 to 28 replicates); hand (30 replicates); and inhalation (28 replicates) exposure values are based on AB grade data. High confidence in the unit exposure value. No protection factors were needed to define the unit exposure value. **PPE:** The same dermal and inhalation data are used as for the baseline coupled with a 50% protection factor to account for the use of an additional layer of clothing and a 5-fold protection factor to account for the use of a dust/mist respirator. Hand (6 replicates) exposure value is based on AB grade data. Low confidence in the unit exposure value. **Engineering Controls:** Data is based on groundboom enclosed cab. Dermal (20 to 31 replicates); hand (16 replicates); and inhalation (16 replicates) exposure values are based on ABC grade data for dermal and hands and AB grade data for inhalation. Medium confidence for hands and dermal and high confidence for inhalation.

a Standard Assumption: 8-hour work day as estimated by HED. BEAD data were not available.

b Acres treated from HED's Science Advisory Council for Exposure, Policy 009.1, "Standard Values for Daily Acres Treated in Agriculture." Health Effects Division, Office of Pesticide Programs, September 2001.

c "Best Available" grades are defined by HED SOP for meeting Subdivision U Guidelines. Best available grades are assigned as follows: matrices with grades A and B data and a minimum of 15 replicates; if not available, then grades A, B and C data and a minimum of 15 replicates; if not available, then all data regardless of the quality and number of replicates. Data confidence are assigned as follows:
High = grades A and B and 15 or more replicates per body part Medium = grades A, B, and C and 15 or more replicates per body part

Table 6. Baseline: Occupational Handler Short- and Intermediate-Term Exposures and Risks at Baseline Attire

Exposure Scenario	Application Rate[a] (lb ai/acre)	Area *Treated*[b] (acres/ day)	Dermal *Unit* Exposure[c] (mg/lb ai)	Inhalation *Unit* Exposure[d] (ug/lb ai)	Short- and *Intermediate*-Term Dermal Dose[e]	Short- and *Intermediate*-Term Dermal MOE[f]	Short- & *Intermediate*-Term Inhalation Dose[g]	*Short-Term* Inhalation MOE[h]	*Intermediate*-Term Inhalation MOE[i]	Combined Short-Term *Dermal* + Inhalation MOE[j]	Combined *Intermediate*-Term Dermal + Inhalation MOE
Mixer/Loader											
Mixing/Loading Liquid Formulations for Aerial Application (1a)	0.5	1200	2.9	1.2	25	0.08	0.01	49	3.9	0.08	0.079
	0.2	1200	2.9	1.2	9.9	0.2	0.0041	120	9.7	0.2	0.2
	0.1	1200	2.9	1.2	5	0.4	0.0021	240	19	0.4	0.39
Mixing/Loading Liquid Formulations for Groundboom Application (1b)	0.5	200	2.9	1.2	4.1	0.48	0.0017	290	23	0.48	0.47
	0.2	200	2.9	1.2	1.7	1.2	0.00069	730	58	1.2	1.2
	0.1	200	2.9	1.2	0.83	2.4	0.00034	1,500	120	2.4	2.4
Applicator											
Applying Sprays with an Airplane (2)	0.5	1200	No Data – see Engineering Controls								
	0.2	1200									
	0.1	1200									
Applying with a Groundboom (3)	0.5	200	0.014	0.74	0.02	100	0.0011	470	38	83	27
	0.2	200	0.014	0.74	0.008	250	0.00042	1,200	95	210	69
	0.1	200	0.014	0.74	0.004	500	0.00021	2,400	190	410	140
Flagger											
Flagging Aerial Spray Applications (4)	0.5	350	0.011	0.35	0.028	73	0.00088	570	46	65	28
	0.2	350	0.011	0.35	0.011	180	0.00035	1,400	110	160	70
	0.1	350	0.011	0.35	0.0055	360	0.00018	2,900	230	320	140

Footnotes:

Note: Baseline mitigation = long sleeve shirt, long pants, shoes, and socks.

a. Application rate taken from dicrotophos label (EPA 5481-448).

b Amount handled per day values from HED's Science Advisory Council for Exposure, Policy 009.1, "Standard Values for Daily Acres Treated in Agriculture." Health Effects Division, Office of Pesticide Programs, September 2001.

c *Dermal unit exposure values from PHED V1.1 Surrogate Exposure Guide dated August 1998.*

d Inhalation unit exposure values from PHED V1.1 Surrogate Exposure Guide dated August 1998.

e Dermal daily dose (mg/kg/day) = [daily unit exposure (mg/lb ai) x application rate (lb ai/acre) x amount handled per day (acres) / body weight (70 kg).

f Dermal MOE = LOAEL (2.0 mg/kg) / daily dose (mg/kg/day).

g Inhalation daily dose (mg/kg/day) = [inhalation unit exposure (μg/lb ai) x application rate (lb ai/A) x amount handled per day (acres) x conversion factor (1 mg/1,000 μg) x 1 inhalation absorption factor] / body weight (70 kg).

h Short-term Inhalation MOE = LOAEL (0.5 mg/kg) / daily dose (mg/kg/day).

i Intermediate-term inhalation MOE = LOAEL (0.04 mg/kg) / daily dose (mg/kg/day).

j Total MOE = 1 / *dermal* MOE + 1 / *inhalation* MOE

Table 7. PPE: Occupational Handler Short- and Intermediate-Term Exposures and Risks with Personal Protective Equipment

Exposure Scenario	Application Rate[a] (lb ai/acre)	Area Treated[b] (acres/ day)	Dermal Unit Exposure[c] (mg/lb ai)		Inhalation Unit Exposure[d] (ug/lb ai)	Short- & Inter-Term Dermal MOE[e]		Baseline Inhalation MOE[f] (with no respirator)		PPE Inhalation MOE (with respirator)		Combined Short-Term Dermal + Inhalation MOE[i]		Combined Intermediate-Term Dermal + Inhalation MOE[i]	
			Gloves	Gloves + Double Layers		Gloves	Gloves + Double Layers	Short-Term	Inter.-Term	Short-Term[g]	Inter.-Term[h]	Gloves + Double Layers + No Respirator	Gloves + Double Layers + Respirator	Gloves + Double Layers + No Respirator	Gloves + Double Layers + Respirator
Mixer/Loader															
Mixing/Loading Liquid Formulations for Aerial Application (1a)	0.5	1,200	0.023	0.017	0.24	10	14	49	3.9	240	19	11	13	3	8
	0.2	1,200				25	34	120	9.7	610	49	27	32	7.6	20
	0.1	1,200				51	69	240	19	1,200	97	54	65	15	40
Mixing/Loading Liquid Formulations for Groundboom Application (1b)	0.5	200				61	82	290	23	1,500	120	64	78	18	48
	0.2	200				150	210	730	58	3,600	290	160	190	45	120
	0.1	200				300	410	1,500	120	7,300	580	320	390	91	240
Applicator															
Applying Sprays with an Airplane (2)	0.5	1,200	No Data; see Engineering Controls												
	0.2	1,200													
	0.1	1,200													
Applying with a Groundboom (3)	0.5	200	0.014	0.011	0.15	100	130	470	38	2,300	190	100	120	29	76
	0.2	200				250	320	1,200	95	5,800	470	250	300	73	190
	0.1	200				500	640	2,400	190	12,000	930	NA (500)	NA (600)	150	380
Flagger															
Flagging Aerial Spray Applications (4)	0.5	350	No Data	0.01	0.07	No Data	80	570	46	2,900	230	70	78	29	59
	0.2	350					200	1,400	110	7,100	570	180	190	73	150
	0.1	350					400	2,900	230	14,000	1,100	NA (350)	NA (390)	150	300

Footnotes:

Note: Personal protective equipment mitigation:

Gloves	Chemical-Resistant Gloves
Double Layers	Double layer body protection
Respirator	Dust/mist filtering respirator
NA	Not applicable – the risks were not a concern at the baseline risk mitigation level

a Application rate taken from dicrotophos label (EPA 5481-448).

b Amount handled per day values from HED's Science Advisory Council for Exposure, Policy 009.1, "Standard Values for Daily Acres Treated in Agriculture." Health Effects Division, Office of Pesticide Programs, September 2001.

c Dermal unit exposure values from PHED V1.1 Surrogate Exposure Guide dated August 1998.

d Inhalation unit exposure values from PHED V1.1 Surrogate Exposure Guide dated August 1998.

e Dermal MOE = LOAEL (2.0 mg/kg) / daily dose (mg/kg/day). Dermal daily dose (mg/kg/day) = [daily unit exposure (mg/lb ai) x application rate (lb ai/acre) x amount handled per day (acres) / body weight (70 kg)..

f See Table 5: Baseline Exposures and Risks

g Short-term Inhalation MOE = LOAEL (0.5 mg/kg) / daily dose (mg/kg/day). Inhalation daily dose (mg/kg/day) = [inhalation unit exposure (μg/lb ai) x application rate (lb ai/A) x amount handled per day (acres) x conversion factor (1 mg/1,000 μg) x 1 inhalation absorption factor] / body weight (70 kg).

h Intermediate-term inhalation MOE = LOAEL (0.04 mg/kg) / daily dose (mg/kg/day). Inhalation daily dose (mg/kg/day) = [inhalation unit exposure (μg/lb ai) x application rate (lb ai/A) x amount handled per day (acres) x conversion factor (1 mg/1,000 μg) x 1 inhalation absorption factor] / body weight (70 kg).

i Total MOE = 1 / dermal MOE + 1 / inhalation

Table 8. Engineering Controls: Occupational Handler Short- and Intermediate-Term Exposures and Risks at Engineering Controls

Exposure Scenario	Application Rate[a]	Area Treated[b]	Eng Con Dermal Unit Exposure (mg/lb ai)[d]	Eng Con Inhalation Unit Exposure (ug/lb ai)[e]	Short- & Inter.-Term Dermal MOE[f]	Short-Term Inhalation MOE[g]	Inter.-Term Inhalation MOE[h]	Combined Short-Term Dermal and Short-Term Inhalation MOE[i]	Combined Intermediate-Term Dermal and Intermediate-Term Inhalation MOE[i]
Mixer/Loader									
Mixing/Loading Liquid Formulations for Aerial Application (1a)	0.5	1,200	0.0086	0.083	27	700	56	26	18
	0.2	1,200	0.0086	0.083	68	1,800	140	65	46
	0.1	1,200	0.0086	0.083	140	3,500	280	130	92
Mixing/Loading Liquid Formulations for Groundboom Application (1b)	0.5	200	0.0086	0.083	160	4,200	340	160	110
	0.2	200	0.0086	0.083	410	11,000	840	390	270
	0.1	200	0.0086	0.083	810	21,000	1,700	780	550
Applicator									
Applying Sprays with an Airplane (2)	0.5	1200	0.005	0.068	47	860	69	44	28
	0.2	1200	0.005	0.068	120	2,100	170	110	69
	0.1	1200	0.005	0.068	230	4,300	340	220	140
Applying with a Groundboom (3)	0.5	200	0.005	0.043	280	8,100	650	270	200
	0.2	200	0.005	0.043	700	20,000	1,600	680	490
	0.1	200	0.005	0.043	1,400	41,000	3,300	1,400	980
Flagger									
Flagging Aerial Spray Applications (4)	0.5	350	0.00022	0.007	3,600	29,000	2,300	3,200	1,400
	0.2	350	0.00022	0.007	9,100	71,000	5,700	8,100	3,500
	0.1	350	0.00022	0.007	18,000	140,000	11,000	16,000	7,000

Footnotes:

Note: Engineering control mitigation:
- 1a, b single layer clothing, chemical resistant gloves, closed mixing
- 2 single layer clothing, no gloves, enclosed cockpit
- 3, 4 single layer clothing, no gloves, enclosed cab

a Application rate taken from dicrotophos label (EPA 5481-448).

b Amount handled per day values from HED's Science Advisory Council for Exposure, Policy 009.1, "Standard Values for Daily Acres Treated in Agriculture." Health Effects Division, Office of Pesticide Programs, September 2001.

d Dermal unit exposure values from PHED V1.1 Surrogate Exposure Guide dated August 1998.

e Inhalation unit exposure values from PHED V1.1 Surrogate Exposure Guide dated August 1998.

f Dermal MOE = LOAEL (2.0 mg/kg) / daily dose (mg/kg/day). Dermal daily dose (mg/kg/day) = [daily unit exposure (mg/lb ai) x application rate (lb ai/acre) x amount handled per day (acres) / body weight (70 kg).

g Short-term Inhalation MOE = LOAEL (0.5 mg/kg) / daily dose (mg/kg/day). Inhalation daily dose (mg/kg/day) = [inhalation unit exposure (μg/lb ai) x application rate (lb ai/A) x amount handled per day (acres) x conversion factor (1 mg/1,000 μg) x 1 inhalation absorption factor] / body weight (70 kg).

h Intermediate-term inhalation MOE = LOAEL (0.04 mg/kg) / daily dose (mg/kg/day). Inhalation daily dose (mg/kg/day) = [inhalation unit exposure (μg/lb ai) x application rate (lb ai/A) x amount handled per day (acres) x conversion factor (1 mg/1,000 μg) x 1 inhalation absorption factor] / body weight (70 kg).

i Total MOE = 1 / dermal MOE + 1 / inhalation MOE

Table 9. Postapplication Exposure/Risk Estimates to Hand Harvesters Following Late-Season Applications of Dicrotophos to Cotton

DAT[a]	Texas			Mississippi			Combined Site Data		
	DFR at 0.5 lb ai/A[b]	Dermal Dose Late-Season[c]	Short- & Int.-Term MOE[d]	DFR at 0.5 lb ai/A[b]	Dermal Dose Late-Season[c]	Short- & Int.-Term MOE[d]	DFR at 0.5 lb ai/A[b]	Dermal Dose Late-Season[c]	Short- & Int.-Term MOE[d]
0	3.2E-01	9.10E-02	21.9	1.4E-01	3.90E-02	50.9	1.7E-01	5.00E-02	40.4
1	2.4E-01	6.80E-02	29.5	8.6E-02	2.50E-02	81.6	1.3E-01	3.70E-02	53.4
2	1.8E-01	5.00E-02	39.8	5.4E-02	1.50E-02	131	9.9E-02	2.80E-02	70.7
3	1.3E-01	3.70E-02	53.7	3.3E-02	9.50E-03	209	7.5E-02	2.10E-02	93.6
4	9.7E-02	2.80E-02	72.4	2.1E-02	6.00E-03	336	5.6E-02	1.60E-02	124
5	7.2E-02	2.00E-02	97.6	1.3E-02	3.70E-03	NA	4.3E-02	1.20E-02	164
6	5.3E-02	1.50E-02	132	8.1E-03	2.30E-03	NA	3.2E-02	9.20E-03	217
7	3.9E-02	1.10E-02	177	5.1E-03	1.40E-03	NA	2.4E-02	7.00E-03	287
8	2.9E-02	8.40E-03	239	3.2E-03	9.00E-04	NA	1.8E-02	5.30E-03	380
9	2.2E-02	6.20E-03	323	2.00E-03	5.60E-04	NA	1.4E-02	4.00E-03	NA

a DAT = days after application
b DFR ($\mu g/cm^2$) = DFR data from MRID No. 44731001, which was conducted using an application rate of 0.5 lb ai/acre.
c Dermal Dose = DFR ($\mu g/cm^2$) x transfer coefficient (2500 cm^2/hr) x exposure time (8 hrs) x conversion factor (1 mg/1,000 μg) / body weight (70 kg).
d Short- and Intermediate-term Dermal MOE = Short- and Intermediate-Term Dermal LOAEL (2.0 mg/kg) / dermal dose (mg/kg/day).

Table 10. Postapplication Exposure/Risk Estimates to Workers and Scouts Following Late-Season Applications of Dicrotophos to Cotton

DAT[a]	Texas			Mississippi			Combined Site Data		
	DFR at 0.5 lb ai/A[b]	Dermal Dose Late-Season[c]	Short- & Int.-Term MOE[d]	DFR at 0.5 lb ai/A[b]	Dermal Dose Late-Season[c]	Short- & Int.-Term MOE[d]	DFR at 0.5 lb ai/A[b]	Dermal Dose Late-Season[c]	Short- & Int.-Term MOE[d]
0	3.2E-01	5.5E-02	37	1.4E-01	2.4E-02	85	1.7E-01	3.0E-02	67
1	2.4E-01	4.1E-02	49	8.6E-02	1.5E-02	136	1.3E-01	2.2E-02	89
2	1.8E-01	3.0E-02	66	5.4E-02	9.2E-03	218	9.9E-02	1.7E-02	118
3	1.3E-01	2.2E-02	90	3.3E-02	5.7E-03	349	7.5E-02	1.3E-02	156
4	9.7E-02	1.7E-02	121	2.1E-02	3.6E-03	NA	5.6E-02	9.7E-03	207
5	7.2E-02	1.2E-02	163	1.3E-02	2.2E-03	NA	4.3E-02	7.3E-03	273
6	5.3E-02	9.1E-03	219	8.1E-03	1.4E-03	NA	3.2E-02	5.5E-03	362
7	3.9E-02	6.8E-03	296	5.1E-03	8.7E-04	NA	2.4E-02	4.2E-03	NA
8	2.9E-02	5.0E-03	399	3.2E-03	5.4E-04	NA	1.8E-02	3.2E-03	NA

a DAT = days after application
b DFR ($\mu g/cm^2$) = DFR data from MRID No. 44731001, which was conducted using an application rate of 0.5 lb ai/acre.
c Dermal Dose = DFR ($\mu g/cm^2$) x transfer coefficient (1500 cm^2/hr) x exposure time (8 hrs) x conversion factor (1 mg/1,000 μg) / body weight (70 kg).
d Short- and Intermediate-term Dermal MOE = Short- and Intermediate-Term Dermal LOAEL (2.0 mg/kg) / dermal dose (mg/kg/day).

Table 11. Postapplication Exposure/Risk Estimates to Workers and Scouts Following Early-Season Applications of Dicrotophos to Cotton

DAT[a]	Texas			Mississippi			Combined Site Data		
	DFR at 0.1 lb ai/A[b]	Dermal Dose Early-Season[c]	Short- & Int.-Term MOE[d]	DFR at 0.1 lb ai/A[b]	Dermal Dose Early-Season[c]	Short- & Int.-Term MOE[d]	DFR at 0.1 lb ai/A[b]	Dermal Dose Early-Season[c]	Short- & Int.-Term MOE[d]
0*	6.4E-02	7.3E-04	2740	2.8E-02	3.1E-04	6360	3.5E-02	4.0E-04	5050

* DAT = 0 represents approximately 12 hours after application

a DAT = days after application

b DFR ($\mu g/cm^2$) = DFR data from MRID No. 44731001, to account for reduced application rate of 0.1 lb ai/acre.

c Dermal Dose = DFR ($\mu g/cm^2$) x transfer coefficient (100 cm^2/hr) x exposure time (8 hrs) x conversion factor (1 mg/1,000 μg) / body weight (70 kg).

d Short- and Intermediate-term Dermal MOE = Short- and Intermediate-Term Dermal LOAEL (2.0 mg/kg) / dermal dose (mg/kg/day).

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Chemical:	**Dimethyl phosphate ester with 3-hydroxy-**
PC Code:	**035201**
HED File Code	**14000 Risk Reviews**
Memo Date:	**11/07/2001**
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