DICROTOPHOS

RISK CHARACTERIZATION DOCUMENT

Occupational and Residential Bystander Exposures
Special Local Need (24c) Registration: Use on Cotton

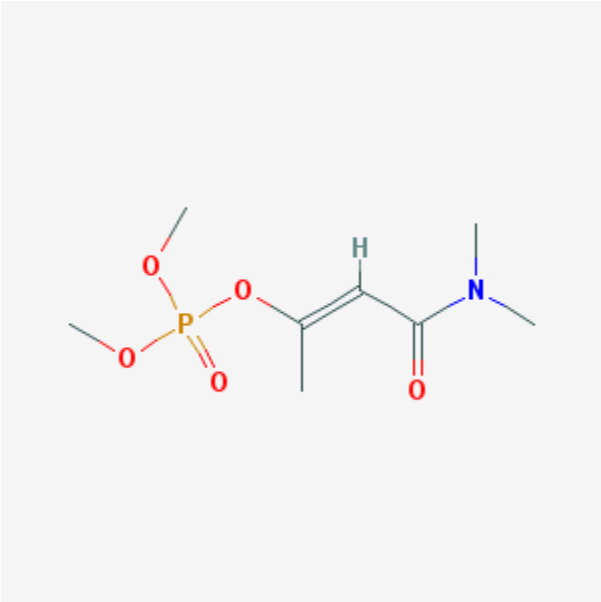

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Table of Contents

CONTRIBUTORS AND ACKNOWLEDGMENTS ii
Table of Contents iii
List of Tables v
SUMMARY vii
I. INTRODUCTION 1
I.A. ENVIRONMENTAL FATE 1
I.A.1. Air 1
I.A.2. Soil 1
I.A.3. Water 2
II. HAZARD IDENTIFICATION 3
II.A. Pharmacokinetics 3
II.B. Neurotoxicity 4
II.B.1. Acute Neurotoxicity Study in Rats 4
II.B.2. Comparative Cholinesterase Studies in Rats 5
II.B.3. 7-Day Oral Exposure in Pre-weanling and Young Adults 7
II.B.4. 28-Day Dermal Exposure in Adult Rats 7
II.B.5. 28-Day Inhalation Exposure in Adult Rats 8
II.B.6. Subchronic Neurotoxicity Study in Adult Rats 9
II.B.7. Developmental Neurotoxicity Study in Rats 9
II.B.8. Rat Chronic Toxicity/Oncogenicity Study 12
II.B.9. Benchmark Dose Analysis of Cholinesterase Inhibition 13
II.C. Weight of Evidence for Carcinogenicity 17
II.C.1. Mouse Oncogenicity Study 17
II.C.2. Rat Combined Chronic Toxicity/Oncogenicity Study 18
II.C.3. Genotoxicity 18
II.C.4. Structure Activity Relationship 20
II.C.5. ToxCast Data 20
II.C.6. Conclusions 21
II.D. Critical Endpoints and Reference Levels 22
III. EXPOSURE ASSESSMENT 23
III.A. Dietary and Drinking Water Exposure 23
III.A.1. Residue Data 23
III.A.2. Software 24

III.A.3. Exposure Estimates 25
III.B. Handler Exposure 26
III.C. Bystander Exposure 27
III.C.1. Adults 27
III.C.2. Children 27
III.D. Aggregate Exposure 28
IV. RISK CHARACTERIZATION 29
IV.A. Diet and Drinking Water 29
IV.B. Handlers 30
IV.C. Bystanders 31
IV.C.1. Adults 31
IV.C.2. Children 32
IV.C.3. Aggregate Exposure 36
V. RISK APPRAISAL 37
V.A. Hazard Identification 37
V.B. Exposure Assessment 38
V.B.1. Dietary and Drinking Water Exposure 38
V.B.2. Occupational and Bystander Exposure 40
V.C. Risk Characterization 40
V.D. U.S. EPA Human Health Risk Assessment for Dicrotophos 41
V.E. Issues Related to the Food Quality Protection Act 45
V.E.1. Pre- and Post-natal Sensitivity 45
V.E.2. Cumulative Toxicity 46
V.E.3. Endocrine Disruption Effect 46
VI. CONCLUSIONS 47
VII. REFERENCES 51
Appendix I. DPR's SB950 Summary of Toxicology Data for Dicrotophos I-1
Appendix II. DPR's SB950 Summary of Toxicology Data for Monocrotophos II-1
Appendix III. Dicrotophos BMD Analysis Summary III-1
Appendix IV. DEEM-FCID Summary Reports for Dicrotophos Dietary and Drinking Water Exposure Assessments IV-1
Appendix V. Human Exposure Assessment for Dicrotophos Used on Cotton V-1

List of Tables

Summary Table 1. Critical Endpoints and NOELs Selected for Evaluating Exposure to Dicrotophos viii
Summary Table 2. Aggregate Margins of Exposure for Handlers xiv
Summary Table 3. Aggregate Margins of Exposure for Adult and Child Bystanders xiv
Table 1. Acute Toxicity Studies for Technical Grade Dicrotophos 5
Table 2. Changes in Neurological Tests and Brain Cholinesterase Activity in Rats after Administration of a Single Dose of Technical Grade Dicrotophos 6
Table 3. Brain Cholinesterase Activity in Pre-weanling and Young Adult Rats after Given a Single Dose of Dicrotophos by Oral Gavage 6
Table 4. Brain Cholinesterase Activity in Pre-weanling and Young Adult Rats after Given Dicrotophos for 7 Consecutive Days by Oral Gavage 7
Table 5. Brain Cholinesterase Activity in Adult Rats after Dermal Exposure to Dicrotophos for 28 Days 8
Table 6. Brain Cholinesterase Activity in Adults Rats after Inhalation Exposure to Dicrotophos for 28 Days 8
Table 7. Changes in Neurological Tests and Brain Cholinesterase Activity in Adult Rats after Dietary Exposure to Dicrotophos for 90 Days 10
Table 8. Changes in Brain Weights in Neonatal Rats in a Neurodevelopmental Toxicity Study for Dicrotophos 11
Table 9. Changes in Brain Morphology in Neonatal Rats in a Neurodevelopmental Toxicity Study for Dicrotophos 12
Table 10. Brain Cholinesterase in Rats Fed Dicrotophos in the Diet for Two Years 13
Table 11. Acute Effects of Dicrotophos and Their Respective NOELs and LOELs 14
Table 12. Short-term and Subchronic Effects of Dicrotophos and Their Respective NOELs and LOELs 15
Table 13. Chronic Effects of Dicrotophos and Their Respective NOELs and LOELs 17
Table 14. Treatment Related Increases in Non-neoplastic and Neoplastic Lesions in Male Mice Fed Dicrotophos in the Diet for Two Years 18
Table 15. Genotoxicity Tests Available for Dicrotophos 19
Table 16. Positive ToxCast Assays for Dicrotophos 21
Table 17. Critical Endpoints and NOELs Selected for Evaluating Exposure to Dicrotophos 23
Table 18. Dietary and Drinking Water Exposure Estimates 26
Table 19. Aggregate Exposures for Handlers 28
Table 20. Aggregate Exposure for Adult and Child Bystanders 29
Table 21. Margins of Exposure for Dietary and Drinking Water Exposure 30
Table 22. Margins of Exposure for Handlers Involved in Application of Dicrotophos to Cotton 31
Table 23. Margins of Exposure for Acute Exposure in Adult Bystanders to Dicrotophos Cotton Spray Drift 33
Table 24. Margins of Exposure for Acute Exposure in Child Bystanders to Dicrotophos Cotton Spray Drift 34
Table 25. Aggregate Margins of Exposure for Handlers 36
Table 26. Aggregate Margins of Exposure for Adult and Child Bystanders 37
Table 27. Comparison of DPR RAS and U.S. EPA HED Critical Endpoints, NOELs/BMDLs and Adjustments Factors for Dicrotophos 43

Table 28. Comparison of Margins of Exposure Calculated by DPR RAS and U.S. EPA HED for Handlers Involved in Application of Dicrotophos to Cotton..... 44
Conclusion Table 1. Aggregate Margins of Exposure for Handlers.....50
Conclusion Table 2. Aggregate Margins of Exposure for Adult and Child Bystanders..... 50

SUMMARY

The Human Health Assessment Branch (HHAB) in the Department of Pesticide Regulation (DPR) conducted a risk assessment for dicrotophos [(E)-4-(dimethylamino)-4-oxobut-2-en-2-yl] dimethyl phosphate, as part of the evaluation for a Special Local Need (SLN) Registration (Section 24c) for Bidrin® 8 (active ingredient = dicrotophos) to be used on cotton for control of brown stink bug. The toxicology database for dicrotophos was reviewed by the Data Review Section (DRS) in HHAB (http://www.cdpr.ca.gov/docs/risk/toxsums/pdfs/72.pdf). The Exposure Assessment Document (EAD) was prepared by the Exposure Assessment Section (EAS) in HHAB (Appendix V). The Toxicology Profile, Hazard Identification, Risk Characterization, and Risk Appraisal were developed by the Risk Assessment Section (RAS).

Hazard Identification

Dicrotophos is an organophosphate pesticide whose primary mechanism of toxicity is cholinesterase inhibition (ChEI). An oral pharmacokinetic study in rats found more than 95% of dicrotophos was absorbed and extensively metabolized. The primary pathway of metabolism starts with cleavage of the phosphate group, with the resultant formation of the acetoacetamide moiety and subsequent hydroxylation of the methyl groups and/or reduction of one of the carbonyl oxygens. ChEI is the most sensitive endpoint for dicrotophos, with higher doses or exposures resulting in overt neurotoxicity (e.g., lacrimation, salivation, fasciculation, chromodacryorrhea). Other effects associated with higher doses that may or may be related to ChEI include reduced body weights, decreased fetal weight, reduced pup viability, reduced fertility index, testicular lesions, and kidney lesions. A number of non-guideline comparative ChEI studies were submitted to DPR which proved useful for selecting critical No-Observed-Effect-Levels (NOELs). The comparative ChEI studies were conducted primarily using the oral route of exposure. However, there was one 28-day dermal ChEI study and one 28-day inhalation ChEI study conducted in adult rats.

A benchmark dose (BMD) analysis was conducted on all brain ChEI studies using exponential models and the Hill model. The lower limit on the BMD which caused 10% ChE inhibition ($BMDL_{10}$) was considered equivalent to a NOEL. The lowest acute $BMDL_{10}$ for brain ChEI was 0.03 mg/kg/day for postnatal day 8 (PND8) pups in the acute oral comparative ChE study in neonates. DPR RAS selected this $BMDL_{10}$ to evaluate children's combined acute oral and dermal exposure to dicrotophos from spray drift onto residential lawns. DPR RAS selected the $BMDL_{10}$ of 2.1 mg/kg/day from the 28-day dermal study in rats to evaluate dermal exposures. DPR RAS assumed a dermal absorption for rats to be 43.7% and adjusted for the differences in exposure duration between the rats and workers (6 hrs vs. 8 hrs). Therefore, 0.69 mg/kg/day became the critical internal dermal NOEL used in evaluating short-term and steady-state dermal exposure in workers. DPR RAS selected the $BMDL_{10}$ of 0.42 µg/L from the 28-day inhalation study in rats to evaluate inhalation exposure. DPR RAS converted this $BMDL_{10}$ to an internal dose by assuming a rat breathes 40 L/kg/hr and 100% inhalation absorption. Therefore, 0.101 mg/kg/day became the critical internal inhalation NOEL was used in evaluating short-term and steady-state inhalation exposure in workers. The BMDLs/NOELs and reference doses/concentrations (RfDs/RfCs) used in this risk assessment are summarized in Summary Table 1.

Summary Table 1. Critical Endpoints and NOELs Selected for Evaluating Exposure to Dicrotophos

Exposure Scenarios	BMDL (Internal NOEL)	RfD/RfC (Internal RfD/RfC)	Effects	Ref. [a]
Oral				
Acute	0.03 mg/kg/day	0.0003	↓ Brain ChEI	1
Steady-State	0.025 mg/kg/day	0.00025	↓ Brain ChEI	2*
Dermal				
All durations	2.1 mg/kg/day (0.92 mg/kg/day)	21 µg/kg/day (9.2 µg/kg/day)	↓ Brain ChEI	3
Inhalation				
All durations	0.43 µg/L (0.101 mg/kg/day)	4.3 ng/L (1.01 µg/kg/day)	↓ Brain ChEI	4
Cancer				
All routes	Limited evidence: Increased thyroid tumors in male mice, no tumor increase in female mice or rats of either gender. Results from genotoxicity tests based on FIFRA guidelines were mixed: negative in reverse mutation assays with *S. typhimurium*, positive in forward mutation with mouse lymphoma assay and negative in micronucleus assay in mouse bone marrow. Evidence was insufficient for a quantitative assessment for cancer.			5* 6* 7* 8* 9*

[a] References: 1. Moxon, 2003a; 2. Horner, 1995; 3. Noakes, 2001; 4. Blair, 2010; 5. Milburn, 1998; 6. Allen, 1998; 7. San and Wyman, 1994; 8. San and Clarke, 1995; 9. Putnam and Young, 1994.
* Study is acceptable to DPR scientists based on FIFRA guidelines.

A statistically significant increase in thyroid tumors was seen in male mice in a 105-week oral oncogenicity study. There was no increase in tumors in female mice or in male or female rats in an oral chronic toxicity/oncogenicity study. Results from the available genotoxicity studies were negative in most assays including several reverse mutation assays with bacteria, two *in vivo* chromosomal assays in bone marrow, a host-mediated assay, and a dominant lethal assay. However, dicrotophos was positive in a mouse lymphoma assay and weakly positive in a reverse mutation assay with yeast. Dicrotophos was tested in the federal Tox21 and ToxCast research programs and was positive in ToxCast assays measuring disruption of immune/inflammatory signaling and inhibition of cytochrome P450 (CYP) enzymes associated with thyroid tumors. DPR RAS concluded there was insufficient evidence of carcinogenicity to calculate cancer potency for dicrotophos.

Exposure Assessment

Dietary and drinking water exposure for various population subgroups were calculated for both acute and steady state exposures. The acute dietary exposure dosages ranged from 1.77 ng/kg/day for adults 50-99 years old to 7.01 ng/kg/day for children 1-2 years old. The steady state dietary dosages were about a third of the acute dosages, ranging from 0.54 ng/kg/day for nursing infants less than one year old to 2.75 ng/kg/day for children 3-5 years old. The acute drinking water dosages ranged from 0.65 ng/kg/day for females of childbearing age to 2.64 ng/kg/day for non-nursing infants less than one year old. The steady state drinking water dosages were much lower ranging from 0.08 ng/kg/day for youths 13-19 years old to 0.53

ng/kg/day for non-nursing infants less than one year old. The acute combined dosages (food and drinking water) ranged from 2.46 ng/kg/day for adults 50-99 years old to 9.13 ng/kg/day for children 1-2 years old. The steady state combined dosages were about one-third to one-quarter of the acute dosages, ranging from 0.42 ng/kg/day for nursing infants less than one year old to 2.85 0ng/kg/day for children 3-5 years old.

Exposure estimates were calculated for handler and bystander scenarios associated with the proposed dicrotophos use on cotton. For handlers, the dermal short-term and seasonal absorbed daily dosages (STADDs and SADDs, respectively) were lowest for scouts (5.05 and 0.301 µg/kg/day, respectively) and highest for mixer/loaders supporting aerial applications (115 and 41.2 µg/kg/day, respectively). The inhalation STADDs and SADDs for handlers were much lower, with ground boom applicators having the lowest exposures (0.208 and 0.0746 µg/kg/day, respectively) and aerial mixer/loaders having the highest exposures (3.75 and 1.35 µg/kg/day, respectively).

Adult bystanders exposure to dicrotophos from spray drift was estimated at various distances from a cotton field for aerial (25-1000 ft.) and ground boom (25-250 ft.) applications using AGDISP and AgDRIFT computer models, respectively. For aerial application, acute inhalation and dermal exposure estimates were calculated using two different application rates (0.25 and 0.5 lb AI/acre) and two types of aircraft (fixed wing AT802A and Bell 205 helicopter). Ground boom application resulted in significantly lower STADDs (0.550 - 3.13 µg/kg/day at 25 ft.) compared to aerial application (5.36 -11.2 µg/kg/day at 25 ft.). The inhalation STADDs for adult bystanders with aerial application were only slightly lower than dermal STADDs ranging from 2.78 to 5.52 µg/kg/day at 25 ft. Dermal and inhalation exposure estimates were similar between aircraft types. Inhalation exposure was not estimated for ground boom application due to insufficient data in the model.

Acute exposures from dicrotophos spray drift were also estimated for child bystanders using dermal, inhalation and 3 different oral exposure pathways (hand to mouth, object to mouth and soil ingestion). The estimates were calculated at various distances from a cotton field (25-1,000 ft) using the AGDISP model with two different application rates and two different types of aircraft for aerial application. Acute exposures were also calculated for ground boom applications using dermal and 3 different oral pathways at various distances from the field (25-250 ft.) using AgDRIFT model with two different application rates at either a high or low boom. The absorbed dermal exposure estimates at 25 ft. away from the field ranged from 7.85-16.5 µg/kg/day with aerial application and 0.368-4.02 µg/kg/day with ground boom application. The inhalation exposures resulting from aerial application ranged from 6.9714.4 µg/kg/day at a distance of 25 ft from the field. Regardless of application method, oral exposures were less than the dermal or inhalation exposures. The lowest exposure at a distance of 25 ft. was soil ingestion (0.0014-0.0029 µg/kg/day aerial, 0.00006-0.00070 µg/kg/day ground boom). The highest exposure was hand-to-mouth activity (0.621-1.30 µg/kg/day aerial, 0.291-0.318 µg/kg/day ground boom). As with adults, the oral and dermal exposure estimates were considerably lower for ground boom application compared to aerial application. Estimates varied for aerial application depending on the aircraft type, but the differences were not great.

Risk Characterization

The risk for threshold effects is expressed as a Margin of Exposure (MOE) which is the ratio of the NOEL or BMDL to the exposure dosage. A combined MOE for all routes can be calculated when exposure occurs by more than one route and route-specific NOELs are used. The combined MOE is the inverse of the sum of the inverses of the MOEs for each route, provided that NOELs for the same or related endpoints were used to calculate the MOE for each route. When the NOEL or BMDL is derived from an animal study, the target MOE is 100, which assumes a default 10-fold uncertainty factor for interspecies variation and another default 10-fold uncertainty factor for intraspecies variation. All the NOELs/BMDLs for dicrotophos are derived from animal studies, so the target MOE for most adult population subgroups is 100.

It is HHAB's practice to consider an additional uncertainty factor when there is evidence of increased sensitivity in young or developing animals or in pregnant animals. The reproductive, developmental, or pup NOELs were all equal to or higher than the maternal or paternal NOELs in the reproductive and developmental toxicity studies. While ChE activity was not measured in all studies, several comparative ChE studies showed significantly higher inhibition in neonates than in young adult rats with either acute or 7-day repeated exposures. Since the acute oral NOEL for ChEI in pre-weanling rats was used to evaluate oral exposure in child bystanders, an additional uncertainty factor for infants and children was not considered necessary. Dermal exposure in child bystanders was evaluated using the NOEL from a 28-day dermal ChE study in adult rats. An additional uncertainty factor for infants and children was not recommended when using this dermal NOEL, since the reduction in the dermal NOEL due to subchronic exposure in adults was considered comparable to the reduction expected in the acute dermal NOEL when measured in neonates rather than adults.

U.S. EPA recently conducted a systematic review of the literature to determine if developmental neurotoxicity is associated with OPs pesticides. Collective results from toxicity studies in animals, mechanistic and human epidemiology studies showed that OPs are active on a number of biological pathways that affect the developing brain. Most of these studies investigated the potential neurodevelopmental effects in infants and children as a result of prenatal exposure to chlorpyrifos. This review identified behavioral effects in animals and associations with neurodevelopmental outcomes such as attention deficit hyperactivity disorder (ADHD), behavioral problems, and autism spectrum in humans. Because of the uncertainty as to whether exposures below those that result in ChE inhibition can still produce developmental neurotoxicity, U.S. EPA retained the Food Quality Protection Act (FQPA) factor of 10 for many OPs including dicrotophos. Based on this systematic review and US EPA's approach, HHAB is also recommending an additional uncertainty factor of 10 be applied when evaluating exposure to infants, children and women of childbearing age due to uncertainty related to the possible developmental neurotoxicity effects. Therefore, HHAB recommends a target MOE of 1000 for these population subgroups.

The dietary and drinking water MOEs for all population subgroups were greater than 1,000 when considered separately or combined with either acute or steady state exposure.

For handlers, the MOEs were less than 100 for dermal exposure for all scenarios except for the seasonal exposure for ground boom mixer/loaders and applicators and scouts. However, the seasonal dermal MOEs for handlers of ground boom application were less than 1,000 while scouts seasonal dermal MOE was greater than 1,000. The inhalation MOEs were greater than 100 but less than 1,000 for most handler scenarios. The scenarios with inhalation MOEs less than 100 included short-term and seasonal exposure for aerial mixer/loaders and short-term exposure for flaggers. On the other end of the spectrum, the seasonal inhalation MOE for ground boom applicators was greater than 1,000. The combined MOEs for handlers were similar to the dermal MOEs since most of their exposure was by the dermal route.

The dermal MOEs for adult bystanders to ground boom applications were all greater than 100 at 25 ft with either low or high boom and both application rates. The dermal MOEs were greater than 1,000 at 250 ft with all ground boom application scenarios. With aerial application, the dermal MOEs were greater than 100 for adult bystanders at 50 ft for all scenarios, but not greater than 1,000 until 1000 ft and only with fixed wing aircraft. The inhalation MOEs were less than 100 for adult bystanders up to 1,000 ft for all scenarios, except when dicrotophos was applied at 0.25 lb AI/acre by helicopter. Even for that scenario the MOE was only slightly greater than 100. The combined MOEs were similar to the inhalation MOEs and were less than 100 at 1,000 ft for all adult bystander scenarios.

The dermal MOEs for child bystanders were all greater than 100 at 100 ft. when dicrotophos was applied aerially, but were less than 1,000 for most scenarios up to 1,000 ft from the field edge except when applied by helicopter at 0.25 lb AI/acre. When applied by ground boom, the child dermal MOEs were greater than 100 at 25 ft for all scenarios, but were not greater than 1,000 for high-boom equipment until 200 ft at 0.5 lb AI./acre. Inhalation MOEs of child bystanders to aerial applications were less than 100 for all distances considered, up to 1,000 ft. The oral MOEs of child bystanders to aerial applications were greater than 100 for hand-to-mouth activity at 500 ft, but still less than 1,000 at 1000 ft from the field edge. All other oral MOEs for child bystanders exceeded 1,000 at 50 ft. With ground boom application, the MOEs for hand-to-mouth activity were greater than 1,000 at 200 ft, except with high boom equipment at 0.5 lb AI/acre. The combined MOEs were similar to the inhalation MOEs for aerial application and were below 100 even at 1,000 ft from the field edge. Some of the combined MOEs for ground boom application were greater than 1,000 at 250 ft., but only with low boom equipment.

Conclusions

The potential for dicrotophos use on cotton to result in adverse health effects in humans was evaluated in this risk assessment.

The dietary and drinking water MOEs for all population subgroups were all greater than 1,000 when considered separately or combined with either acute or steady state exposure.

The dermal MOEs for handlers were less than the target of 1000 for female workers of childbearing age for all scenarios. The handlers MOEs were even less than 100 for all scenarios except for scouts, so this exposure is a concern even for adult males.

The inhalation MOEs for handlers was greater than 100 for most scenarios except aerial mixer/loaders (short-term and steady-state) and flaggers (short-term only). However, the inhalation MOEs were less than 1,000 for all scenarios except seasonal exposure for ground boom applicators so they are a concern for female workers of reproductive age. The combined dermal and inhalation MOEs were similar to the dermal MOEs since dermal exposure was much greater (Summary Table 2).

The dermal MOEs for adult bystanders were all greater than 100 at 25 ft with ground boom application and with aerial application when applied at 0.25 lb AI/acre. The dermal MOEs were greater than 1,000 at 250 ft for all ground boom scenarios and at 1,000 ft. with aerial application at 0.25 lb AI/acre. With aerial application, the inhalation MOEs for all adult bystander scenarios were less than 100 even at 1,000 ft., except when applied by helicopter at 0.25 lb AI/acre. None of the inhalation MOEs were greater than 1,000 at 1,000 ft.

The dermal, inhalation and oral MOEs for child bystanders were all greater than 1,000 with ground boom application using a low boom at 100 ft. from the field edge. With high boom equipment, child bystanders did not have MOEs greater than 1,000 at even 250 ft. from the field edge when applied at 0.5 lb AI/acre. With aerial application, child bystanders inhalation MOEs were below 100 even at 1,000 ft. from the field edge. Dermal MOEs for most child bystander scenarios were also less than 1,000 even at 1,000 ft. Oral MOEs tended to be higher, but some activities like hand-to-mouth activity had MOEs that were still less than 1,000 at 1,000 ft from the field edge (Summary Table 3).

Risk Appraisal

Dietary exposure represented the "high-end" of the potential exposure because it was based on a deterministic approach using average residues from residue studies on unprocessed undelinted whole cottonseed and it assumed that 100% of the crop was treated. The use of pesticide residue data from the US Department of Agriculture (USDA) Pesticide Data Program (PDP) on finished drinking water may lead to an underestimation of the exposure, because PDP may not detect peak pesticide concentrations in drinking water. The DPR surface and ground water programs currently do not monitor dicrotophos since is not registered for use in California.

The MOEs for acute dermal and inhalation exposure in workers and adult bystanders were based on NOELs/BMDLs for subchronic dermal and inhalation studies. Comparison of the oral acute and subchronic NOELs/BMDLs indicate the acute NOELs/BMDLs were 3 to 20 fold higher than the subchronic NOELs/BMDLs. Based on these differences with oral NOELs/BMDLs, the acute dermal and inhalation NOELs/BMDLs and MOEs for dicrotophos are likely to be 3 to 20 fold higher than estimated from the 28-day studies by these routes. On the other hand, the dermal NOEL/BMDL is probably 2 to 7 fold lower in infants and children than for adults based on comparisons of the oral NOELs/BMDLs for brain ChEI in pups and adults.

Therefore, the acute dermal NOEL/BMDL in neonates is probably close to the subchronic dermal NOEL/BMDL in adult rats, which was used for evaluating child bystander exposure.

U.S. EPA and HHAB calculations would occasionally generate different results for the BMD analysis of the brain ChE data because U.S. EPA only used the exponential model and HHAB included the Hill model, which often provided a better fit. Both agencies selected the same study and endpoint to evaluate acute oral exposure in children, but HHAB derived a BMDL of 0.03 mg/kg/day using the Hill model, which is 2-fold lower than the BMDL of 0.07 mg/kg/day derived by U.S. EPA with the exponential model.

U.S. EPA and HHAB obtained the same BMDL for the 28-day dermal study using the exponential model, but U.S. EPA multiplied the BMDL by the ratio of the *in vitro* dermal absorption rate in rats to humans (4.44) to obtain a "Refined Dermal Equivalent Dose (RDD)" for humans. Using the same studies, HHAB estimated different dermal absorption rates for rats and humans by including the residues in the epidermis and stratum corneum in the "absorbed dose." In addition, HHAB used an upper end estimate of the in vivo human dermal absorption to adjust the exposure dosages because in vivo human dermal absorption was not actually measured. The ratio of the *in vivo* dermal absorption in rats to humans used by DPR was approximately 1.7. This difference in dermal absorption assumptions resulted in U.S. EPA's dermal MOEs being approximately 3-fold higher than DPR's.

U.S. EPA and HHAB obtained different BMDLs for the 28-day inhalation study using the same exponential model because U.S. EPA assumed 10 animals/sex/dose when only 5 animals/sex/dose had ChE activity measured. In addition, different breathing rate assumptions were made when converting the BMDL expressed as air concentration to mg/kg/day (U.S. EPA - 43.5 L/kg/hr; HHAB - 40 L:/kg/day). These differences resulted in U.S. EPA's inhalation NOEL being 75% higher than DPR's inhalation NOEL.

In addition to differences in assumptions about dermal absorption, DPR's handler MOEs for dicrotophos were significantly different from U.S. EPA's because: 1) HHAB used upper confidence limits on both the 95th and mean exposure estimates whereas U.S. EPA used the mean; 2) U.S. EPA used the Agricultural Handler Exposure Task Force (AHETF) database while HHAB used the Pesticide Handler Exposure Database (PHED) to estimate handlers exposure.

Summary Table 2. Aggregate Margins of Exposure for Handlers

Scenario	Acute			Seasonal		
	Combined MOE [a] Occupation	Combined MOE Diet+Water	Combined MOE Total	Combined MOE Occupation	Combined MOE Diet+Water	Combined MOE Total
Aerial Appplication						
Mixer/loaders	5	10,000	5	14	28,000	14
Applicators	8	10,000	8	21	28,000	20
Flaggers	3	10,300	3	9	28,000	9
Ground Application						
Mixer/loaders	29	10,000	29	82	28,000	82
Applicators	75	10,000	74	210	28,000	210
Post-application						
Scouts	140	10,000	130	2,300	28,000	2,100

[a] MOE: Margin of Exposure = [NOEL or BMDL]/Exposure. Combined MOE = $1/(1/MOE_{dermal}+1/MOE_{inhalation})$. The $BMDL_{10}$ for dermal exposure was 2.1 mg/kg/day. The absorbed dermal NOEL was 0.69 mg/kg/day. The $BMDL_{10}$ for inhalation exposure was 0.42 µg/L . The absorbed inhalation NOEL is 0.101 mg/kg/day. The $BMDL_{10}$ for oral acute exposure is $BMDL_{10}$ is 0.03 mg/kg/day. The $BMDL_{10}$ for seasonal/steady-state exposure is 0.025 mg/kg/. For more details see Table 25. Occupational exposure dosages are from Tables 4-6 in the EAD for dicrotophos (Appendix V). Dietary and drinking water exposure dosages are from Table 20 in this RCD.

Target MOE = 1000

Summary Table 3. Aggregate Margins of Exposure for Adult and Child Bystanders

Rate (lb/A)	Equipment	Adult			Child		
		Combined MOE [a] Drift	Combined MOE Diet+Water	Combined MOE Total	Combined MOE Drift	Combined MOE Diet+Water	Combined MOE Total
Aerial Application at 1000 ft.							
0.25	**Fixed wing**	86	10,000	85	31	3,300	31
	Helicopter	95	10,000	95	35	3,300	35
0.50	**Fixed wing**	60	10,000	60	22	3,300	21
	Helicopter	68	10,000	68	25	3,300	25
Ground Application at 250 ft.							
0.25	**Fixed wing**	3,900	10,000	2,800	980	3,300	750
	Helicopter	8,600	10,000	4,700	3,500	3,300	1,700
0.50	**Fixed wing**	1,900	10,000	1,600	490	3,300	420
	Helicopter	4,300	10,000	3,000	1,800	3,300	1,100

[a] MOE = Margin of Exposure = NOEL or BMDL/Exposure. Combined MOE = $1/(1/MOE_{dermal}+1/MOE_{inhalation})$. The BMDL10 of 2.1 mg/kg/day was used to evaluate dermal exposure. MOE was calculated using the absorbed dermal NOEL of 918 µg/kg/day. The $BMDL_{10}$ for inhalation exposure is 0.42 µg/. The absorbed inhalation NOEL is 0.101 mg/kg/day. The $BMDL_{10}$ for acute oral exposure is 0.03 mg/kg/day. For more details see Table 26. Bystander exposure dosages are from Tables 7-9 in the EAD (Appendix V). Dietary and drinking water exposure dosages are from Table 18 in this RCD.

Target MOE=1000

I. INTRODUCTION

Dicrotophos (dimethyl phosphate of 3-hydroxy-N,N-dimethyl-cis-crotonamide) is an organophosphate pesticide that is currently not registered for use in California. Dicrotophos was first registered in the United States in 1964 by Shell Oil Company as a contact systemic insecticide for use on cotton and various seed crops (U.S. EPA, 2006a). In 1972, a registration was issued for use as a tree injection treatment on ornamental and non-crop trees. The registration for tree injection treatment is a repackaging of formulated product. This registration is held by J.J. Mauget Company. In October 1986, the Shell Oil Company transferred dicrotophos registrations to DuPont Corporation, and in January 1994, registrations were transferred to Amvac Chemical Company. A Registration Standard was issued for dicrotophos in 1982. A Data-Call-In (DCI) was issued for reregistration in 1991. The California Cotton Ginners and Growers Association submitted a Special Local Need (SLN) registration (section 24c) for Bidrin® 8 which is manufactured by Amvac Chemical Corp. to be used on cotton for control of brown stink bug. The physical/chemical properties, formulation, usage, and illness reports are discussed in the exposure assessment document (EAD, Appendix V) for this 24c registration of dicrotophos and will not be discussed here.

I.A. ENVIRONMENTAL FATE

I.A.1. Air

Dicrotophos is not expected to volatilize from water surfaces or from moist soil surfaces based on the Henry's Law constant of 3.13-5.03 x 10^{-11} atm-m^3/mole (U.S. EPA, 1998; HSDB, 2016). Dicrotophos is not likely to volatilize from dry soil surfaces based on the reported low to moderate vapor pressures ranging from of 4.7 x 10^{-6} mm Hg (U.S. EPA, 1998) to 1.6 x 10^{-4} mm Hg (HSDB, 2016). If released to air, dicrotophos will exist in both the vapor and particulate phases in the atmosphere. Vapor-phase dicrotophos will be degraded by reaction with photochemically-produced hydroxyl radicals and ozone. Half-lives are estimated to be 7.4 and 24 hours, respectively (HSDB, 2016). Because dicrotophos contains chromophores that absorb at wavelengths > 290 nm, direct photolysis is possible. However, photolysis studies at the soil surface and in aqueous environments showed that degradation is not induced by light exposure (HSDB, 2016). Particulate-phase dicrotophos is removed from the atmosphere by wet or dry deposition.

I.A.2. Soil

The K_{oc} for dicrotophos in Georgia sandy soil, Handford sandy loam, Catlin silty loam, and Sharkey clay loam are 16, 53, 43, and 188, respectively, indicating very high to moderate mobility in soil (HSDB, 2016). U.S. EPA reported very similar K_{oc} values in sand, sandy loam, silt loam and clay soils of 11, 53, 40 and 187, respectively (U.S. EPA, 1998). Dicrotophos is classified as a non-persistent pesticide with an estimated soil half-life of less than 0.5 months; dicrotophos granules applied to field soils have an initial half-life of a few days (HSDB, 2016). In laboratory persistence studies using ^{14}C labeled dicrotophos in sandy loam soil, half-lives of 3 and 7 days were observed under aerobic and anaerobic conditions, respectively.

In an aerobic soil metabolism study, the half-life for dicrotophos was 2.6 days in Hanford sandy loam soil incubated in the dark at 25°C for 14 days (U.S. EPA, 1998). The major degradates

were N,N-dimethylacetoacetamide (20%) and CO_2 (58%). The unextracted soil residues represented 26.5% of applied dose. The anaerobic soil metabolism half-life was 7 days in the same soil incubated in the dark at 25°C for 33 days. The major degradates of anaerobic metabolism were N,N-dimethylacetoacetamide (48%) and its hydroxyl derivative (13%), and CO_2 (18%). The unextracted residues with anaerobic soil metabolism were only 6.2% of the applied radioactivity.

I.A.3. Water

The water solubility of dicrotophos is quite high at 100,000 ppm (U.S. EPA, 1998). Dicrotophos decomposition in water occurs primarily by hydrolysis. Half-lives for the hydrolysis of dicrotophos were 117, 72, and 28 days at pH 5, 7, and 9 at 25°C, respectively (U.S. EPA, 1998; HSDB, 2016). Hydrolysis rates of dicrotophos in aqueous and soil environments are pH-dependent and follow first-order kinetics. Degradation of aqueous dicrotophos is not affected by exposure to UV light. The major hydrolytic degradation products are N,N-dimethylacetoacetamide and O-desmethyldicrotophos (U.S. EPA, 1998). An estimated bioconcentration factor (BCF) of 3 and log K_{ow} of 0.00 indicates low potential for bioconcentration in aquatic organisms (HSDB, 2016).

As part of the Pesticide Contamination Prevention Act (PCPA or AB2021), DPR established Specific Numerical Values (SNVs) for identifying potential ground water contaminants (Bergin, 2014). Pesticides that exceeded these SNVs (water solubility > 3 ppm, K_{oc} < 1900 cm^3/g, hydrolysis half-life > 14 days, aerobic half-life > 610 days and anaerobic half-life > 9 days) may be placed on the Groundwater Pollution List (GWPL) if their application method also involves (1) application or injection into the soil by ground-based application equipment or by chemigation or (2) application followed within 72 hrs by flood or furrow irrigation. The registrants had submitted some environmental fate studies in 1986, but a number of these were not acceptable to DPR and have not been replaced by newer acceptable studies because dicrotophos is not currently registered in California. However, the water solubility, hydrolysis rate and K_{oc} values reported by U.S. EPA and/or HSDB exceed DPR's SNVs and indicate potential risk of groundwater contamination. Even though dicrotophos exceeds some of these SNVs, it is not currently on DPR's GWPL since there are no registered uses.

Over 4,649 well samples from the National Water-Quality Assessment Program (NAWQA) were tested for dicrotophos (Troiano, 2016). Two samples had detectable residues of 0.0429 and 0.0232 µg/L. These detections are suspect because they were below the reporting limit (0.0843 µg/L) and collected from wells in Iowa where cotton is not grown. There were zero detections of dicrotophos among 2,677 samples taken from drinking wells greater than 50 feet deep.

The United States Geological Survey (USGS) measured levels of pesticides and herbicides used in cotton farming in surface water samples collected from January to December 1996 from the Mississippi Embayment (Thurman *et al.*, 1998). Dicrotophos was the most frequently detected pesticide, with 35% of the samples testing positive. Of the 60 samples analyzed, 13 were positive for dicrotophos. The median detected dicrotophos concentration was 0.1 ppb, the maximum was 0.2 ppb and the minimum was 0.02 ppb. The limit of detection for these GC-MS analyses was 0.01 ppb.

Since dicrotophos is not registered in California, it is not routinely tested for in surface or well water monitored by DPR. However, a query of the Water Quality Portal (WQP) database maintained by the USGS California Water Science Center and California State Water Resources Control Board (SWRCB) for the National Water Quality Monitoring Council found no dicrotophos detections among 781 surface water samples from California that were analyzed between 2000-2014 (USGS, 2016). The detection limits for most samples were within 0.08 to 0.0843 µg/L, although some were as low as 0.016 µg/L.

The California Environmental Data Exchange Network (CEDEN) database maintained by SWRCB was also queried for surface water monitoring data for dicrotophos (SWRCB, 2016). In the CEDEN database there were 1,353 samples analyzed for dicrotophos between 2001 and 2011. Among these samples, 13 samples had trace detections of dicrotophos, 12 of which were below the laboratory reporting limit of 0.05 µg/L and one sample was just above the reporting limit at 0.06 ug/L. Nine of these trace detections were from the Calleguas Creek watershed in Ventura County and the other four were from various streams in San Diego County. A query of the Pesticide Use Report found only one reported use of dicrotophos for the entire state in 2002 which involved 1,000 applications on one day on rights of way in San Diego County totaling 26.9 lbs (DPR, 2016). This may be a case where the product number was incorrectly reported since dicrotophos was not registered for use in California at that time and the small amount involving multiple applications on one day suggests it was applied to pots in a nursery[1].

II. HAZARD IDENTIFICATION

U.S. EPA completed a human health assessment for dicrotophos in July 2014 and updated it in September of 2015 (U.S. EPA, 2014a, 2015a). These assessments were reviewed by HHAB and compared to current practices. U.S. EPA determined the database was complete for dicrotophos, including standard acute and subchronic neurotoxicity studies, developmental neurotoxicity study, chronic toxicity studies, oncogenicity studies, developmental studies, and a reproductive study. In addition, the registrant performed a subchronic immunotoxicity study, subchronic dermal and inhalation studies, and acute and subchronic comparative ChE studies. Several the studies that were considered critical to the evaluation of its neurotoxic and carcinogenic potential will be discussed in more detail in this section as well as the pharmacokinetics. These include the acute and subchronic neurotoxicity studies, the comparative cholinesterase studies in pups and young adults, developmental neurotoxicity study and cholinesterase studies with dermal and inhalation exposure.

II.A. Pharmacokinetics

In a pharmacokinetics study in rats with oral dosing of radiolabeled dicrotophos, the primary route of excretion was the urine (86 to 89% of dose administered after 4 days of collection) with only 1.5 to 5% excreted in the feces (Wu and Gu, 1996). These data indicated that approximately 94 to 97% of the oral administered dose was absorbed. In the metabolite analysis,

[1] Email communication from John Troiano, Research Scientist III, Ground Water Program, Environmental Monitoring Branch, California Department of Pesticide Regulation.

the parent compound constituted only 3 to 7% of the administered dose. The formation of monocrotophos by demethylation of one of the amide methyl groups was <1 to 3% of the dose. Cleavage of the phosphate group with the resultant formation of the acetoacetamide moiety and subsequent hydroxylation of the methyl groups and/or reduction of one of the carbonyl oxygens was the primary pathway of metabolism.

Two dermal absorption studies were submitted for dicrotophos, one that measured the dermal absorption *in vivo* in rats (Gledhill, 1999) and the other measured *in vitro* dermal absorption in rats and humans (Davies, 1999). The in vitro dermal absorption was calculated by adding the residues in the acceptor fluid to those in the epidermis and stratum corneum. In vivo dermal absorption was the sum of the residues in the stratum corneum and skin, urine, feces, GI tract contents, carcass, cage wash, carbon dioxide trap, and charcoal trap. Based on these residues, the mean *in vivo* rat dermal absorption at 24 hrs was 43.7%. This value was used to adjust the rat dermal NOEL to an absorbed dose. The 95% confidence interval (CI) for the *in vivo* dermal absorption in humans was estimated from these two studies assuming the variation in the human dermal absorption is similar to the variation in the rat *in vivo* and *in vitro* dermal absorption (Ngo, 2015). The estimated 95% CI for human *in vivo* dermal absorption was 26.3%. This estimate was used to convert the occupational and bystander dermal exposure doses to absorbed doses.

II.B. Neurotoxicity

As an organophosphate pesticide the primary mechanism of toxicity is inhibition of the enzyme, acetylcholinesterase (AChE), in the central and peripheral nervous systems that is involved in the termination of nerve impulses between certain types of nerves. The cholinergic signs observed in laboratory animals after acute exposure to dicrotophos include lacrimation, salivation, fasciculation, chromodacryorrhea, unkempt appearance and abnormal posture. At necropsy of animals that died, discolored liquid in the stomachs and minor hemorrhages in the cranial cavity or brain surface were observed. In addition, acute inhalation exposure increased breathing depth, reduced breathing rate, and caused irregular breathing and abnormal respiratory noise. The acute toxicity studies of technical grade dicrotophos are summarized in Table 1. These studies were not considered in selecting the critical NOEL since they used high doses and did not measure cholinesterase inhibition (ChEI), which is one of the more sensitive endpoints for dicrotophos.

II.B.1. Acute Neurotoxicity Study in Rats

Groups of 10 Wistar rat/sex/dose were given a single dose of technical grade dicrotophos (87.65% purity) by gavage in at 0 (distilled water), 0.5, 5 or 10 mg/kg (Rattray, 1995). A satellite group of 10 rats/sex/group were dosed similarly from which 5 rats/sex/dose were euthanized at 3 hrs and 8 days for ChE measurements. Functional observational batteries (FOBs) were performed a week prior to dosing, day 1 (2-3 hrs post-dosing), 8 and 15. Besides assessment of neurobehavioral changes in the cage and open field, the functional observational battery (FOB) included tests for auditory startle response, landing foot splay, time to tail flick and grip strength were performed.

Table 1. Acute Toxicity Studies for Technical Grade Dicrotophos

Study Type	Species	Result	Category	Reference [a]
Oral LD_{50}	Rat	11 mg/kg (M) 8 mg/kg (F)	I	1*
Dermal LD_{50}	Rat	876 mg/kg (M) 487 mg/kg (F)	II	1*
Inhalation LC_{50}	Rat	>0.061 mg/L (M/F)	II	2*
Primary Eye Irritation	Rabbit	Mild irritation	III	1*
Primary Dermal Irritation	Rabbit	No irritation	IV	1*
Dermal Sensitization	Guinea pig	Sensitization	NA	1*

[a] References: 1.Price, 1985; 2. Noakes, 2004.
*The study was acceptable to DPR toxicologists based on FIFRA guidelines

Motor activity was also assessed at this time in an automated activity recording device. One male and 3 females dosed with 10 mg/kg died within 3 hours of dosing. Bodyweight and food consumption were reduced during the first week after dosing. Various cholinergic signs were observed in FOB on the day of dosing at 5 and 10 mg/kg including ataxia, flaccidity, reduced foot withdrawal reflex, decreased pupillary response to light, salivation, shaking, tip toe gait, upward curvature of the spine, chromodacryorrhea, and urinary incontinence. Tail flick response, grip strength and motor activity were also affected in both sexes at 5 and 10 mg/kg on Day 1 (Table 2). Brain ChE was inhibited in a dose-related manner at all treatment levels (Table 2) Erythrocyte and plasma ChE were also inhibited at these dose levels, but the toxicological significance of their inhibition is less certain. In this study the brain ChEI was the most sensitive endpoint with a NOEL less than 0.5 mg/kg. This study was acceptable to DPR based on Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) guidelines.

II.B.2. Comparative Cholinesterase Studies in Rats

II.B.2.a. Acute Oral Exposure in Pre-weanling and Young Adults

Moxon (2003a) examined the cholinesterase inhibition in pre-weanling rats by administering a single dose of dicrotophos (90.4% purity) by gavage at 0, 0.1, 0.3, 1 or 5 mg/kg to 5 Alpk:AP_fSD rats/sex/dose of three age groups, postnatal day (PND) 8, 15, and 22. Pups were euthanized 2 hours after dosing and cholinesterase activity was measured in brain and red blood cells (RBCs). One male PND8 pup at 5 mg/kg died on Day 1. All pups at 5 mg/kg had tremors and other cholinergic signs. The signs were more evident in PND15 pups. The clinical signs in the lower dose groups were limited to slight tremors in one male PND8 pup at 1 mg/kg. Only the brain cholinesterase activity is shown in Table 3. Statistically significant brain ChEI was observed in both sexes at all age groups from 0.3 to 5 mg/kg. Slight brain ChEI was also seen at 0.1 m g/kg in some age groups. RBC ChEI was also seen at all dose levels except for PND8 pups at 0.1 mg/kg. This study was a non-guideline study, but was considered scientifically valid by DPR toxicologists.

Table 2. Changes in Neurological Tests and Brain Cholinesterase Activity in Rats after Administration of a Single Dose of Technical Grade Dicrotophos [a]

Neurological Test Day 1	Dose Level (mg/kg)			
	0	0.5	5	10
Males				
Time to tail flick (s)	4.7±2.4	7.2±2.6	12.8±5.5**	19.9±0.3**
Grip strength (g)				
Forelimb	793±131	750±162	560±97**	386±88**
Hindlimb	410±88	425±101	340±82	231±56**
Motor activity [b]	277.5±162.9	254.6±135.6	134.6±68.**2	88.0±41.7**
Brain ChE (IU/g)	10.48±0.71	8.13±0.77**	1.95±0.32**	1.08±0.26
Females				
Time to tail flick (s)	6.9±2.0	7.0±2.5	16.0±5.3**	18.5±2.9**
Grip strength (g)				
Forelimb	688±120	763±94	643±92	371±51**
Hindlimb	395±66	453±90	320±93*	250±41**
Motor activity [b]	351.4±177.7	415.0±168.0	73.7±41.0**	84.3±82.2**
Brain ChE (IU/g)	10.57±0.51	8.40±0.29**	2.02±0.31**	1.00±0.39**

[a] Rattray, 1995.
[b] Number of recordable actions during session.
*,** Significantly different by pairwise comparison with controls using a two-sided Student's t-test ($p < 0.05$ and 0.01, respectively).

Table 3. Brain Cholinesterase Activity in Pre-weanling and Young Adult Rats after Given a Single Dose of Dicrotophos by Oral Gavage

Brain ChE Activity (IU/g)	Dose Level (mg/kg)					Ref. [a]
	0	0.1	0.3	1	5	
Males						
PND [b]8	3.39±0.28	2.83±0.23**	1.95±0.17**	1.14±0.20**	0.64±0.07**	1
PND15	4.69±0.38	3.73±0.60**	2.95±0.18**	1.48±0.25**	0.77±0.04**	1
PND22	5.18±0.31	4.79±0.69	4.38±0.48**	2.28±0.11**	1.16±0.18**	1
PND42	4.77±0.27	4.99±0.32	4.57±0.60	-----	1.24±0.09**	2
Females						
PND8	3.19±0.26	2.99±0.09	2.09±0.26**	1.17±0.18**	0.66±0.05**	1
PND15	4.90±0.30	3.31±0.45**	2.69±0.10**	1.40±0.17**	0.77±0.04**	1
PND22	5.43±0.44	4.41±0.26**	4.02±0.31**	2.51±0.35**	1.33±0.19**	1
PND42	5.22±0.63	4.76±0.19	4.07±0.24**	-----	1.26±2.06**	2

[a] References: 1. Moxon, 2003a; 2. Brammer, 2002a.
[b] PND = Postnatal Day
** Significantly different by pairwise comparison with controls ($p < 0.01$)

Cholinesterase inhibition was also examined in groups of 5 young adult Alpk:AP_fSD rats/sex/dose give a single dose of dicrotophos (87.6% purity) by gavage at 0, 0.1, 0.3 or 5 mg/kg and euthanized at 3 different times points after dosing (Day 1 - 3 hrs post-dosing, Day 8 and Day 15) (Brammer, 2002a). Cholinergic signs were only observed on the first day in rats at 5 mg/kg and included tremors, splayed gait, reduced stability, spine curved upward, irregular breathing and decreased activity and pinched-in sides. Small reductions in food consumption and body weights were also observed during the first week at this dose level. Significant brain ChEI was seen at 0.3 mg/kg in females and in both sexes at 5.0 mg/kg (Table 3). RBC ChE measured and inhibition was less than that observed in the brain. The NOEL was 0.1 mg/kg in young adult rats, but less than 0.1 mg/kg based on brain ChEI. This was a non-guideline study, but was considered scientifically valid by DPR toxicologists.

II.B.3. 7-Day Oral Exposure in Pre-weanling and Young Adults

Differences in ChEI was also examined in 5 pre-weanling and young adult Alpk:AP_fSD rats/sex/dose after receiving dicrotophos (90.4% purity) by gavage for 7 days at 0, 0.008, 0.2, 0.08 or 0.4 mg/kg in phase I and 0 or 1.0 mg/kg in phase II (Moxon, 2003b). Rats were sacrificed 2 hrs after the last treatment. Brain ChEI was observed in both sexes in both age groups at 0.4 and 1.0 mg/kg with slightly greater inhibition in pre-weanling rats (Table 4). RBC ChEI was seen in both sexes of pre-weanling rats at 0.08 and 0.4 mg/kg/day. RBC ChEI was only inhibited in young adult rats at 0.4 mg/kg/day. No clinical signs were seen in pre-weanling or young adult rats at any dose level tested. The NOEL was 0.08 mg/kg/day in both age groups based on brain ChEI. This was a non-guideline study that was considered scientifically valid by DPR toxicologists.

Table 4. Brain Cholinesterase Activity in Pre-weanling and Young Adult Rats after Given Dicrotophos for 7 Consecutive Days by Oral Gavage [a]

Brain ChE (IU/g)	Dose Level (mg/kg)				
	0	0.008	0.02	0.08	0.4
Males					
PND[b]12-18	4.84±1.34	4.06±0.38	4.85±1.11	4.09±0.95	2.41±0.18**
PND42-48	4.57±0.54	4.87±0.97	5.24±0.13	4.75±0.48	3.35±0.34**
Females					
PND12-18	4.46±0.41	4.14±0.46	4.41±1.07	3.79±0.29	1.89±0.20**
PND42-48	5.01±0.45	4.70±0.53	5.70±0.65	5.01±0.30	3.19±0.27**

[a] Moxon, 2003b.
[b] PND = Postnatal Day
** Significantly different by pairwise comparison with controls ($p < 0.01$).

II.B.4. 28-Day Dermal Exposure in Adult Rats

Dicrotophos (87.6% purity) was applied to the of 15 Crl:CD rats/sex/dose for 6 hours/day, 5 days/week for 28 day period (Noakes, 2001). Several mortalities occurred during the study including one control female, one female at 2 mg/kg, one male at 5 mg/kg/day, one male and 4 females at 80 mg/kg/day between study days 18 and 21. The investigator did not consider these deaths to be treatment related because they occurred prior to the animals being dosed, and

instead attributed the deaths to poor bandaging. No changes in neurobehavioral activity were seen in the FOB or in the motor activity assessment. The only clinical sign that was dose related was erythema in females at all treatment levels. Erythema was not seen in any of the males. There was no treatment-related effect on body weight in the main study groups, was reduced in the males 80 mg/kg/day ChE satellite group. No effect on food consumption, ophthalmological findings, hematology or clinical chemistry values except cholinesterase activity. Cholinesterase activity in the brain, RBCs, and plasma was measured in five animals/sex/dose at the study termination. Dose-related decreases in brain, RBC and plasma ChE were seen at 10 and 80 mg/kg/day. RBC ChE inhibition was seen in males at 2 and 5 mg/kg/day in males, but not females. Plasma ChE inhibition was seen in females at 2 and 5 mg/kg/day, but not males. Only brain ChE activity is shown in Table 5. No treatment changes in organ weights or histopathological findings were observed. The NOEL for this study was 5 mg/kg/day based on brain ChEI. This study was acceptable according to FIFRA guidelines.

Table 5. Brain Cholinesterase Activity in Adult Rats after Dermal Exposure to Dicrotophos for 28 Days [a]

Brain ChE (IU/g)	Dose Level (mg/kg/day)				
	0	2	5	10	80
Males	5.10±0.42	4.61±0.42	4.84±0.55	3.71±0.65*	2.21±0.39**
Females	5.09±1.15	4.32±0.47	4.46±0.97	3.76±0.18*	1.76±0.18**

[a] Noakes, 2001
*,** Significantly different by pairwise comparison with controls ($p < 0.05$ or 0.01, respectively)

II.B.5. 28-Day Inhalation Exposure in Adult Rats

Ten Crl:CD rats/sex/dose were exposed nose-only to dicrotophos (88.9% purity, 90-99% vapor or < 7 µm) at 0, 0.097, 0.73 and 2.9 µg/L (analytical) for 6 hours/day, 5 days/week for 4 weeks (Blair, 2010). There were no mortalities or treatment-related changes in clinical signs, body weights and food consumption. The only hematological effect was a reduction in reticulocytes in males at 2.9 µg/L. No treatment related changes in clinical signs were seen except ChEI which measured in RBCs and brain. Brain ChEI was seen at 0.73 and 2.9 µg/L in both sexes and in females at 0.097 µg/L (Table 6). RBC ChEI was also seen at these same dose levels with similar levels of inhibition, although inhibition in females at 0.097 µg/L was not statistically significant. There was no treatment related effect on organ weights, but atrophy of the seminiferous tubules was seen in males at 2.9 µg/L. The NOEL for this study was 0.097 µg/L for males and less than 0.097 µg/L for females based on the brain ChEI. This study was a non-guideline study, but was considered scientifically valid by DPR toxicologists.

Table 6. Brain Cholinesterase Activity in Adults Rats after Inhalation Exposure to Dicrotophos for 28 Days [a]

Brain ChE (U/g) [b]	Dose Level (µg/L)			
	0	0.097	0.73	2.9
Males	23.32±1.50	23.29±0.87	20.67±0.46**	15.16±0.58**
Females	24.43±1.67	22.84±0.61*	20.68±0.62**	15.09±0.84**

[a] Blair, 2010
[b] x 10^3
*,** Significantly different by pairwise comparison with controls ($p < 0.05$ or 0.01, respectively).

II.B.6. Subchronic Neurotoxicity Study in Adult Rats

In a subchronic neurotoxicity study, 12 Alpl:AP_fSD rats/sex/dose were fed dicrotophos technical (87.65% purity) in the diet at 0, 0.05, 5 or 25 ppm (males: 0, 0.04, 0.39 or 2.03 mg/kg/day; females: 0, 0.04, 0.45 or 2.38 mg/kg/day, respectively) for 13 weeks (Horner, 1995). Two satellite cohorts of 6 rats/sex/dose/cohort were treated in the same manner, except they were euthanized at 5 and 9 weeks and ChE activity was measured in the plasma, RBCs and brain. FOBs were performed on all animals in the main study at weeks -1, 5, 9 and 14. Besides neurobehavioral assessments in the cage and open field, the FOB included tests for auditory startle response, landing foot splay, time to tail flick, and grip strength. At the same time their overall motor activity was assessed in an automated activity recording device. Animals in the satellite groups were subjected to observations in the cage and open field, but not measurements of reflexes, strength and motor activity. A reduction in body weights and food consumption was seen in both sexes at 25 ppm during the first week. In the FOB, a decreased pupillary response was seen in 5/17 males and 2/18 females at week 9 at 25 ppm. This was the only time this effect was noted. Forelimb and hindlimb grip strength was slight reduced at 25 ppm week 9 (Table 7). At week 14, this effect was less apparent. Motor activity was also reduced at 25 ppm at week 9, but persisted through week 14 (Table 7). Brain ChEI was seen in both sexes at all time points tested (Table 7). There were no treatment-related lesions seen with gross or microscopic examination. The NOEL for this study was less than 0.5 ppm (M/F: 0.04 mg/kg/day), the lowest dose tested. This study was acceptable to DPR toxicologists based on FIFRA guidelines.

II.B.7. Developmental Neurotoxicity Study in Rats

Groups of 30 time-mated female Wistar rats/dose (F_0 generation) were administered dicrotophos (87.65% purity) by gavage at 0, 0.01, 0.05 or 0.4 mg/kg/day from gestation day (GD) 7 through PND 7 (Brammer, 2003). The pups (F_1 generation) were then administered dicrotophos directly by oral gavage from PND8 through PND22. An FOB was performed on the F_0 dams on GD 10 and 17 and lactation day (LD) 2 and 9. FOBs were performed on 10 F_1 pups/sex/dose (1 male and 1 female from each litter) on days PND 5, 12, 22, 36, 46, and 61. Motor activity was measured in one male and one female pup from each littler on PND 14, 18, 22 and 60. The auditory startle response was also assessed in one male and one female pup from each litter on PND 23 and 61. Tests of learning and memory were performed on PND 21, 24, 59 and 62 in one male and one female from each litter. There were no treatment related effects on body weights and clinical signs in either the dams or pups. There were also no treatment-related differences in motor activity, startle response or learning and memory. Pre-pubertal separation of the vaginal opening was also not affected in the female pups. A statistically significant increase in absolute brain weights was seen in female pups on PND 12 at all dose levels and in perfused brains only on PND 63 at 0.4 mg/kg/day (Table 8). The brain to body weight ratio, however, was not significantly different and tended to trend in the other direction. When an analysis of covariance was performed with body weight as a covariate, the brain weights adjusted for body weight were significantly higher at 0.4 mg/kg/day. No significant increases in absolute brain weights were seen in unperfused brains of females on PND 63 or in any male treatment groups on either PND 12 or 63. Brain morphometric measurements were performed only in control groups and at 0.4 mg/kg/day on PND 12 and 63. Significant differences in some measurements were seen in both sexes on PND 12 and 63, but the direction of change (increased or decreased) or regions affected

were not consistent within or between sexes or days (Table 8). Since these measurements were not performed at the low and mid doses, it is uncertain if these changes were treatment-related or random differences. No treatment- related differences in the histopathological lesions in the brain were seen. In general, DPR does not consider changes in organ weights without associated clinical signs or histopathological changes to be toxicological significant. However, out of an abundance of caution, the significant increase in brain weight relative to body weight at 0.4 mg/kg/day was used in this risk assessment. The neurodevelopmental NOEL for this study is 0.05 mg/kg/day. The maternal NOEL is 0.4 mg/kg/day. This study is considered acceptable based on FIFRA guidelines.

Table 7. Changes in Neurological Tests and Brain Cholinesterase Activity in Adult Rats after Dietary Exposure to Dicrotophos for 90 Days [a]

Neurological Endpoint		Dose Level (mg/kg/d)			
		0	0.1	0.3	1
Males					
Grip strength	Wk 5 - forelimb hindlimb	1396±215 983±172	1331±153 1015±116	1342±210 904±120	1196±156* 873±122
	Wk 9 - forelimb hindlimb	1386±236 675±163	1496±174 623±189	1481±220 610±183	1335±206 629±80
	Wk 14 - forelimb hindlimb	1464±235 759±235	1442±214 800±164	1288±224* 788±191	1408±208 800±125
Motor Activity	Wk 5	390.8±94.2	426.5±111.9	384.3±113.0	351.2±139.4
	Wk 9	506.0±192.5	498.9±109.4	508.8±132.5	333.3±140.1**
	Wk 14	466.9±146.2	506.3±151.8	397.6±119.8	365.0±165.1
Brain ChE (IU/g)	Wk 5	11.00±0.95	9.82±0.68**	4.13±0.36**	1.21±0.08**
	Wk 9	10.64±0.76	8.53±0.54**	4.24±0.30**	1.18±0.33**
	Wk 14	9.83±0.50	8.57±0.34**	4.30±0.43**	1.25±0.08**
Females					
Grip strength	Wk 5 - forelimb - hindlimb	1069±112 738±107	1092±180 800±106	1138±206 733±108	965±144 704±95
	Wk 9 - forelimb - hindlimb	1135±116 400±55	1092±169 367±61	1121±95 421±108	985±141** 335±56*
	Wk 14 - forelimb - hindlimb	1192±178 548±130	1090±123 573±149	1233±174 515±140	1027±136* 552±192
Motor activity	Wk 5	528.6±87.2	574110.0.8±	535.2±114.4	459.6±125.8
	Wk 9	496.1±140.5	524.5±159.1	486.6±149.6	380.3±121.9*
	Wk 14	529.5±123.5	502.0±137.7	474.0±113.7	357.4±108.6*
Brain ChE (IU/g)	Wk 5	9.66±1.07	8.44±0.78*	3.82±0.54**	1.09±0.30**
	Wk 9	10.80±1.17	9.38±0.56**	3.95±0.39**	1.07±0.10**
	Wk 14	10.70±0.87	9.16±0.66**	4.00±0.38**	1.23±0.10**

[a]Horner, 1995.
*,** Significantly different by pairwise comparison with controls (p , 0.05 or 0.01, respectively).

Table 8. Changes in Brain Weights in Neonatal Rats in a Neurodevelopmental Toxicity Study for Dicrotophos [a]

Neurological Endpoint	Dose Level (mg/kg/day)			
	0	0.01	0.05	0.4
Males				
Terminal body wts – PND[b] 12	23.2±2.5	22.7±3.5	23.0±4.1	24.1±1.4
Brain wts – PND 12				
Absolute	1.19±0.04	1.11±0.09	1.10±0.09	1.13±0.04
Relative to body wt	4.80±0.43	4.93±0.43	4.84±0.54	4.68±0.26
Adjusted for body wt.	1.11	1.12	1.10	1.11
Terminal body wts – PND 63	351.1±18.7	341.6±27.5	352.1±21.0	359.8±16.6
Brain wts – PND 63				
Absolute	1.98±0.07	2.00±0.06	1.99±0.07	2.02±0.05
Relative to body wt	0.56±0.02	0.59±0.04	0.57±0.03	0.56±0.02
Adjusted for body wt	1.98	2.01	1.99	2.01
Terminal body wts – PND 63 Perfused	350.3±22.2	357.5±26.9	348.6±30.2	357.2±26.9
Brain wts, perfused – PND 63				
Absolute	2.01±0.09	1.99±0.09	1.99±0.11	2.03±0.09
Relative to body wt	0.58±0.05	0.56±0.04	0.57±0.04	0.57±0.05
Adjusted for body wt	2.01	1.98	1.99	2.02
Females				
Terminal body wts – PND 12	21.0±3.1	22.4±2.4	24.0±2.6	24.1±3.4
Brain wts – PND 12				
Absolute	1.03±0.08	1.08±0.07*	1.09±0.04*	1.12±0.05**
Relative to body wt	4.95±0.45	4.86±0.33	4.59±0.44	4.72±0.48
Adjusted for body wt.	1.06	1.09	1.07	1.10†
Terminal body wts – PND 63	210.5±13.4	218.6±19.2	214.3±16.0	222.9±14.1
Brain wts – PND 63				
Absolute	1.86±0.05	1.87±0.04	1.85±0.04	1.88±0.06
Relative to body wt	0.89±0.07	0.86±0.07	0.87±0.06	0.85±0.06
Adjusted for body wt	1.87	1.86	1.85	1.87
Terminal body wts – PND 63 Perfused	209.0±23.4	219.2±19.3	216.6±18.6	228.8±20.4
Brain wts, perfused – PND 63				
Absolute	1.77±0.07	1.81±0.06	1.80±0.09	1.85±0.06**
Relative to body wt	0.85±0.08	0.83±0.07	0.84±0.05	0.81±0.07
Adjusted for body wt	1.78	1.80	1.80	1.83

[a] Brammer, 2003.
[b] PND = Postnatal Day
*,** Significantly different from controls by pairwise comparison (p , 0.05 or 0.01, respectively).
† Significantly different by analysis of covariance with body weight as the covariate. Differences from controls were tested comparing least squares mean for control and treatment groups using a two-sided Student's t-test.

Table 9. Changes in Brain Morphology in Neonatal Rats in a Neurodevelopmental Toxicity Study for Dicrotophos [a]

Neurological Endpoint	Dose Level (mg/kg/day)			
	0	0.01	0.05	0.4
Males				
Brain Morphology – PND[b] 12				
Frontal cortex				
Level 2 - height	6.29±0.75	-----	-----	5.41±0.63**
- width	4.99±0.52	-----	-----	4.34±0.56*
Dorsal Cortex				
Level 4 – thickness	1.27±0.09	-----	-----	1.16±0.10*
Brain morphology – PND 63				
Thalmus/cortex				
Level 4 – overall width	14.44±0.35	-----	-----	13.74±0.82
Females				
Brain Morphology – PND 12				
Dorsal Cortex 1				
Level 3 – thickness	1.42±0.09	-----	-----	1.33±0.12*
Hippocampus, dentate gyrus				
Level 4 - Width	0.49±0.05	-----	-----	0.53±0.03*
- Length	1.30±0.06	-----	-----	1.39±0.13*
Level 5 - Width	0.70±0.10	-----	-----	0.77±0.05*
- Overall width	1.33±0.13	-----	-----	1.43±0.07*
Brain morphology – PND 63				
Hippocampus				
Level 3 - Length from midline	2.64±0.24	-----	-----	2.35±0.15**
Thalmus				
Level 4 - Width	8.27±0.34	-----	-----	7.92±0.38*

[a] Brammer, 2003.
[b] PND = Postnatal Day
*,** Significantly different from controls by pairwise comparison (p , 0.05 or 0.01, respectively).

II.B.8. Rat Chronic Toxicity/Oncogenicity Study

Fifty-two Alpk:AP$_f$SD rats/sex/dose were fed dicrotophos at 0, 0.5, 5.0 or 25 ppm for 105 weeks (Allen, 1998). There were two satellite cohorts of 12 rats/sex/dose and 16 rats/sex/dose that were euthanized at 53 and 105 weeks, respectively, for ChE analysis in the plasma, RBCs and brain. Rats of both sexes exhibited neurological signs at 25 ppm including aggressive behavior (males), irregular breathing, abnormal respiratory noise (females), involuntary shaking, hunched posture, urine staining and piloerection (females). Females at 5 ppm also had urine staining. Survival was significant reduced in males at 5 and 25 ppm so that all surviving males at these dose levels were sacrificed at weeks 100 and 97, respectively. Survival in females at 25 ppm was also reduced, but 29% survived to week 105. ChEI was seen in plasma, RBCs and brain in both sexes at 0.5 ppm and above (Table 10). This study was acceptable to DPR toxicologists based on FIFRA guidelines.

Table 10. Brain Cholinesterase in Rats Fed Dicrotophos in the Diet for Two Years [a]

Brain ChE (IU/g)	Dose Level (ppm)			
	0	0.1	0.3	1
Males				
Week 53	10.7±0.13	8.63±0.58**	4.26±0.29**	1.26±0.38**
Week 100	8.93±0.64	7.84±0.48**	3.37±0.47**	-----
Females				
Week 53	11.4±0.8	8.78±1.77**	5.03±1.89**	1.42±0.30**
Week 105	8.37±0.70	6.83±0.63**	3.55±1.26**	0.78±0.17**

[a] Allen, 1998.
** Significantly different from controls by pairwise comparison with controls ($p < 0.01$).

II.B.9. Benchmark Dose Analysis of Cholinesterase Inhibition

Tables 11-13 summarize the animal toxicity studies available for dicrotophos by duration of exposure. Among these studies, the developmental toxicity, developmental neurotoxicity, reproductive toxicity and mouse oncogenicity studies did not measure ChE activity. As can be seen from these tables, the ChEI is the most sensitive endpoint when measured with all durations of exposure. NOELs were often not observed for the brain ChEI which made benchmark dose analysis (BMD) of this endpoint useful. U.S. EPA did an extensive BMD analysis of the brain ChEI for many of these studies. U.S. EPA limited their BMD analysis to the four exponential models using the relative deviation and a benchmark response (BMR) of 10% for brain or RBC ChEI. This is based on the approach they used with the cumulative risk assessment for organophosphate pesticides (U.S. EPA, 2002, 2006b). U.S. EPA did not report a BMD analysis for the acute neurotoxicity study in rats and the chronic toxicity study in dogs. Therefore, a BMD analysis was performed on these two studies for this risk assessment for comparison with U.S. EPA's BMD analysis for other studies using the same approach (relative deviation and BMR=10%). This analysis was limited to the brain ChEI and did not include RBC or plasma ChEI. HHAB's practice is to use RBC ChEI as a surrogate of the inhibition in target tissues in humans if brain measurements are not available. In addition, a BMD analysis was performed on the brain ChEI data from the subchronic neurotoxicity studies to compare results from the exponential models with the other continuous models to see if other models fit the data better.

Table 11. Acute Effects of Dicrotophos and Their Respective NOELs and LOELs

Species	Exposure Duration	Effects	NOEL *BMDL*[b]	LOEL *BMD*	Ref [a]
			mg/kg/day		
Oral					
Rat [c]	Single, gavage	↓ Brain ChE	--- *0.21 (M)* *0.18 (F)*†	0.5 (M/F) *0.25 (M)* *0.24 (F)*†	1*
Rat [d]	Single, gavage	PND[e] 8; ↓ Brain ChE	--- (M) *0.03 (M)*† 0.1 (F) *0.06 (F)*†	0.1 (M) *0.05 (M)*† 0.3 (F) *0.09 (F)*†	2
		PND 15: ↓ Brain ChE	--- (M/F) *0.07 (M)* *NAF (F)*	0.1 (M/F) *0.08 (M)* *NAF (F)*	
		PND 22: ↓ Brain ChE	0.1 (M) *0.13 (M)* --- (F) *NAF (F)*	0.3 (M) *0.23 (M)* 0.1(F) *NAF (F)*	
Rat [d]	Single, gavage	PND 42; ↓ Brain ChE	0.3 (M) *0.22 (M)* 0.1 (F) *0.09 (F)*	5.0 (M) *0.38 (M)* 0.3 (F) *0.12 (F)*	3

[a] References: 1. Rattray, 1995; 2. Moxon, 2003a; 3. Brammer, 2002a.
[b] Red italics are the benchmark dose lower limit (BMDL) and benchmark dose (BMD) for the model with the best fit for the endpoint shown. Yellow highlighting indicates the endpoint and BMDL selected for the critical NOEL.
[c] Acute neurotoxicity study
[d] Non-guideline study comparative ChE study.
[e] Postnatal Day
*The study was acceptable to DPR toxicologists based on FIFRA guidelines.
†BMD analysis resulted in a better fit with Hill model.
NAF = No acceptable fit by BMD analysis with all four exponential models and Hill model.

After the initial analysis of these 3 studies, it was noted that the Hill model often fit the data better than any of the exponential models. The other three models (linear, power, and polynomial) rarely had a better fit. Since the Hill model is based on the Michaelis-Menten equation that best describes receptor binding kinetics, it was concluded that this model should be included in the BMD analysis for brain ChEI along with the exponential models. Therefore, for this risk assessment a BMD analysis was conducted on all the available studies with brain ChEI data using all four exponential models and the Hill model.

The results from the BMD analysis for brain ChEI are included in Tables 11-13 in red italics under the NOEL and LOEL. The results shown are for the model with the best fit based on the highest p-value for Test 4 (model fit), lowest AIC score, smallest scaled residuals and best fit visually, in that order. Appendix III summarizes the results of the batch runs for each set of data with the p-values for Tests 1-4, AIC score, scaled residuals and BMD and BMDL. When the p-

Table 12. Short-term and Subchronic Effects of Dicrotophos and Their Respective NOELs and LOELs

Species	Exposure Duration	Effects	NOEL *BMDL*[b]	LOEL *BMD*	Ref [a]
			mg/kg/day		
Oral					
Rat [c]	7 Days, gavage	PND 12-18: ↓ Brain ChE PND 42-48: ↓ Brain ChE	0.08 (M/F) *0.03 (M)* *0.03 (F)* 0.08 (M/F) *0.05 (M)* *NAF (F)*	0.4 (M/F) *0.06 (M)* *0.05 (F)* 0.4 (M/F) *0.11 (M)* *NAF (F)*	3
Rat [d]	GD [c] 6-15, gavage	Maternal: Clinical signs, ↓body wt. gain Fetal: No effects	0.5 2.0 (HDT)	1.0 ---	1*
Rabbit [d]	GD5-29, gavage	Maternal: Clinical signs Fetal: ↓ Body weights	0.1 1.0	0.5 2.0	2*
Rat [e]	Maternal: GD7-, LD7, Pups: PND8 21, both gavage	Maternal: No adverse effects Pups: ↑ Brain wt adjusted for body wt	0.4 (HDT) 0.05	--- 0.4	4*
Rat [c]	28 Days, gavage	↓ Brain ChE	0.02 (M) *0.015 (M)* 0.008 (F) *0.004 (F)*[†]	0.4(M) *0.060 (M)* 0.02 (F) *0.011 (F)*[†]	5
Rat [f]	28 Days, Diet	↓ Brain ChE (males only tested)	---	0.37 (M/F)	6*
Rat [c]	28 Days, gavage 56 Days, gavage	↓ Brain ChE ↓ Brain ChE	--- ---	0.4 0.4	7
Rat [g]	90 Days. diet	Wk 5: ↓ Brain ChE Wk 9: ↓ Brain ChE Wk 14: ↓ Brain ChE	--- (M/F) *0.036 (M)* *0.026 (F)*[†] --- (M/F) *NAF (M)* *0.025 (F)*[†] --- (M/F) *0.031 (M)*[†] *0.025 (F)*[†]	0.04 (M/F) *0.039 (M)* *0.032 (F)*[†] 0.04 (M/F) *NAF (M)* *0.029 (F)*[†] 0.04 (M/F) *0.034 (M)*[†] *0.029 (F)*[†]	8*
Rat [h]	2-Gen., 2-litter, 10-wk premating	Parental: ↓ Body weights (M/F) Pups: ↓ Viability Reproductive: ↓ Fertility index	0.05-0.06 0.05-0.06 1.25	0.49-0.59 0.53-0.59 1.29-2.46	9*

Table 12 (cont.). Subchronic Effects of Dicrotophos and Their Respective NOELs and LOELs

Species	Exposure Duration	Effects	NOEL *BMDL*[b]	LOEL *BMD*	Ref [a]
			mg/kg/day		
Dermal					
Rat [c]	28 Days 6 hrs/day, 5 days/wk	↓ Brain ChE	5.0 (M/F) *3.50 (M)*† *2.13 (F)*	10.0 (M/F) *8.52 (M)*† *3.35 (F)*	10
Inhalation (µg/L)					
Rat [c]	28 Days, 6 hrs/day, 5 days/wk	↓ Brain ChE	0.097 (M) *0.43 (M)* --- (F) *0.41 (F)*†	0.73 (M) *0.58 (M)* 0.097 (F) *0.48 (F)*†	11

[a] References: 1. Rodwell, 1986; 2. Moxon, 2001; 3. Moxon, 2003b; 4. Brammer, 2003; 5. Brammer, 2002c; 6. Arrowsmith, 2011; 7 Brammer, 2002b; 8. Horner, 1995; 9. Moxon, 1997; 10. Noakes, 2001; 11. Blair, 2010.
[b] Red italics are the benchmark dose lower limit (BMDL) and benchmark dose (BMD) for the model with the best fit for the endpo shown. Yellow highlighting indicates the endpoint and BMDL selected for the critical NOEL
[c] Non-guideline ChE study
[d] Developmental toxicity study
[e] Developmental neurotoxicity study
[f] Immunotoxicity study
[g] Subchronic neurotoxicity study
[h] Reproductive toxicity study
* The study was acceptable to DPR DRS based on FIFRA guidelines.
† BMD analysis resulted in a better fit with Hill model.
NA = No acceptable fit by BMD analysis with all four exponential models and the Hill model.

value for Test 3 was less than 0.10 (indicating the non-homogeneous variance was not modeled well), but the Test 4 p-value was greater than 0.10 (indicating good model fit), the BMD and BMDL estimates for this model was still considered acceptable to DPR. In a few cases (females in 28-day inhalation study and males in 28-day dermal study), the Test 4 p-value was less than 0.1, but close (0.088 and 0.092, respectively) and was considered acceptable given that the alternative was to use a NOEL approach.

When the results from the Hill model resulted in a better fit, the BMD and BMDL were flagged with a dagger symbol (†). The Hill model resulted in a better fit in the acute comparative ChE study with male and female PND8 pups. The Hill model also resulted in a better fit in the acute neurotoxicity study (females) and in the subchronic neurotoxicity study (females at wk 5, wk 9 and wk 14 and males at wk 14). In addition, the Hill model resulted in a better fit in the 28-day oral toxicity study (females), in the 28-day dermal toxicity study (males) and in the 28-day inhalation study (females). HHAB also obtained different BMD and BMDL values than U.S. EPA for the 28-day inhalation study using the exponential models because U.S. EPA assumed 10 rats/sex/dose in their analysis when only 5 rats/sex/dose had the ChE activity measured in this study. Also, with the males, U.S. EPA entered the mean ChE activity incorrectly for the top dose. Finally, the Hill model had a better fit in the 2-year rat chronic toxicity/oncogenicity study in females at wk 53 and in both sexes at weeks 100 (males)/105 (females).

Table 13. Chronic Effects of Dicrotophos and Their Respective NOELs and LOELs

Species	Exposure Duration	Effects	NOEL *BMDL*[b]	LOEL *BMD*	Ref [a]
			mg/kg/day		
Oral					
Mouse	2 Years, diet	↓ Body weight (M/F), ↑ tubular vacuolation in kidneys (M), ↓ survival (F)	1.12 (M) 1.58 (F)	6.42 (M) 9.06 (F)	1*
Rat	2 Years, diet	Wk 53: ↓ Brain ChE	--- (M) *NAF (M)* --- (F) *0.025 (F)*†	0.02 (M) *NAF (M)* 0.03 (F) *0.037 (F)*†	2*
		Wk 100: ↓ Brain ChE	--- (M) *0.019 (M)*†	0.02 (M) *0.024 (M)*†	
		Wk 105: ↓ Brain ChE	--- (F) *0.023 (F)*†	0.03 (F) *0.032 (F)*†	
Dog	1 Year, diet	↓ Brain ChE	--- (M/F) *0.034 (M)* *0.072 (F)*	0.025 (M/F) *0.069 (M)* *0.100 (F)*	3*

[a] References: 1. Milburn, 1998; 2. Allen, 1998; 3. Horner, 1997.
[b] Red italics are the benchmark dose lower limit (BMDL) and benchmark dose (BMD) for the model with the best fit for the endpoint shown. Yellow highlighting indicates the endpoint and BMDL selected for the critical NOEL
*The study was acceptable to DPR DRS based on FIFRA guidelines.
†BMD analysis resulted in a better fit with Hill model.

II.C. Weight of Evidence for Carcinogenicity

II.C.1. Mouse Oncogenicity Study

Fifty-five C57BL/10J$_f$CD-1 Alpk mice/sex/dose were fed dicrotophos in their diet at 0, 5, 10 or 50 ppm, for 105 weeks (Milburn, 1998). There were transient reductions in food consumption and body weights at 50 ppm in both sexes during the first few weeks of exposure. The survival of females at 50 ppm was reduced such that the remaining females were all euthanized on day 101. There were no treatment related effects on ophthalmological and hematological findings. With the histopathological examination, a dose related increase in renal tubular vacuolization was seen in males that was significant by trend analysis ($p < 0.001$), but not pairwise comparison to controls probably due to the high background incidence (Table 14). Males also had a dose-related increase in follicular cell adenomas of the thyroid gland that was statistically significant by trend analysis ($p < 0.001$) and by pairwise comparison using Fisher's exact test ($p< 0.05$) (Table 14). Female mice in this study did not have a significant increase in either of these lesions, but they did have a reduced survival rate which could have affected the incidence of tumors. This study was acceptable based on FIFRA guidelines.

Table 14. Treatment Related Increases in Non-neoplastic and Neoplastic Lesions in Male Mice Fed Dicrotophos in the Diet for Two Years [a]

Lesion	Dose Levels (ppm)			
	0	2	10	30
Kidney Tubular vacuolation	23/55[+++] (42%)	23/55 (42%)	31/55 (56%)	39/55 (71%)
Thyroid Follicular cell adenoma	0/54[+++] (0%)	0/53 (0%)	1/53 (2%)	5/49* (10%)

[a] Milburn, 1998.
[+++]Significant trend by Cochran-Armitage trend test ($p < 0.001$).
*Significantly different from control group by pairwise comparison with controls ($p < 0.05$).

II.C.2. Rat Combined Chronic Toxicity/Oncogenicity Study

No increase in tumors of any type were seen in rats (52 Alpk:AP_fSD rats/sex/dose) fed dicrotophos at 0, 0.5, 5.0 or 25 ppm for 105 weeks (Allen, 1998). A satellite cohort of 12 rats/sex/dose were used for an interim sacrifice at 53 weeks. Survival was significantly reduced in males at 5 and 25 ppm so that all surviving males at these dose levels were sacrificed at weeks 97 and 100, respectively. Survival decreased in females at the 25 ppm dose, although 29% survived to week 105. The reduced survival in both sexes could have reduced the tumor incidence in treatment groups, as well. Body weights and food consumption were reduced at 25 ppm during the first few weeks of the study, but subsequently recovered in the females. Male body weights continued to be lower than the controls throughout the study. Although some statistical differences in clinical chemistry and hematology were seen at 25 ppm, there was no consistent effect which exhibited a physiologically significant response. A reduction in urine volume and an increase in specific gravity were seen in both sexes at 25 ppm. There was no treatment related effect on organ weights. The only histopathological lesions noted were an increase in focal atrophy/degeneration of the acinar epithelium of the Harderian gland and aspiration pneumonia in females at 25 ppm. This study was acceptable to DPR toxicologists based on FIFRA guidelines

II.C.3. Genotoxicity

The genotoxicity tests available for dicrotophos are summarized in Table 15. Three acceptable guideline studies were submitted to DPR. Two of the assays were negative including a reverse mutation assay with *Salmonella typhimurium* strains TA98, TA100, TA1535, TA1537 and TA1538 (San and Wyman, 1994) and an *in vivo* micronucleus assay in mouse bone marrow (Putnam and Young, 1994). A mouse lymphoma forward mutation assay with L5178Y $TK^{+/-}$ cells was positive with an increased mutation frequency with and without activation (San and Clarke, 1995). Several older pre-guideline genotoxicity studies for dicrotophos were also submitted by the registrants. Most showed negative results, including reverse mutation assays with *Escherichia coli* B/r WP2 strain (Dean, 1971), *Serratia marcescens* HYα13, HYα21 and CD/rc_3α742 strains and *S. typhimurium* TA1535, TA1536, TA1537 and TA1538 strains (Dean *et al.*, 1974), a chromosomal aberrations assay in bone marrow cells of 4 CF1 mice/sex/dose after a single oral dose of dicrotophos (Dean and Senner, 1973), a host-mediated assay where 1-3 CF1 mice/dose were injected with *Saccharomyces cerevisiae* D4 strain and then given a dose of

dicrotophos (Dean *et al.*, 1974), and a dominant lethal assay in 12 male CF1 mice/dose after a single or repeated oral doses (Dean, 1974). Results for the reverse mutation assays with *E. coli* (Dean, 1971), *S. marcescens*, and *S. typhimurium* (Dean *et al.*, 1974) were considered qualitative since no details were provided. These results were consequently not included in Table 15. Results from the reverse mutation assay with *S. cerevisiae* D4 strain were included in Table 15 because more details were provided for this assay and dicrotophos was weakly mutagenic in this assay (Dean, 1971).

Table 15. Genotoxicity Tests Available for Dicrotophos

Assay/Organism	Concentrations	S-9	Results	Reference
Mutagenicity				
Reverse mutation/ *S. cerevisiae* D4	5, 8, 10, 20 or 50 µg/ml	-	+/-	Dean *et al.*, 1974
Reverse mutation/ *S. typhimurium* TA100	0.5, 5, 50 500 or 5000 µg/plate	+/-	+	Breau *et al.*, 1985
Reverse mutation/ *S. typhimurium* TA98, TA100, TA1535, TA1537 & TA1538	0, 100, 333, 1000, 3333 or 5000 µg/plate	+/-	-	San and Wyman, 1994*
Reverse mutation/ *S. typhimurium* TA97a, TA98, TA100, TA102, & TA1535	0.5, 5, 50, 500, and -5000 µg/plate	+/-	+ at 5000 µg/plate	Wu *et al.*, 2010
Forward mutation/ mouse lymphoma L5178Y $TK^{+/-}$ cells	0, 100, 500, 750, 1000, 2000 or 3000 µg/ml	+/-	+	San and Clarke, 1995*
Chromosomal Damage				
Chromosomal aberrations/ 4 CF1 mice/sex/dose bone marrow	0, 5 or 10 mg/kg orally	NA [a]	-	Dean and Senner, 1973
Micronucleus assay/ 5 ICR mice/sex/dose/time bone marrow	0, 1.7, 3.3 or 6.6 mg/kg (i.p.)	NA	-	Putnam and Young, 1994*
Chromosomal aberrations/ CHO-K1 cells	0.375, 0.75 or 1.5 µM	+/-	+ all doses	Wu *et al.*, 2010
Sister chromatid exchange/ CHO cells	0.03, 0.1, 0.3 or 1.0 mM	NR	+	Nishio and Uyeki, 1981
Other Genotoxicity Assays				
Host-mediated/ 1-3 CF1 mice/dose injected i.p. with *S. cerevisiae* D4	0, 5, 10 400 mg/kg orally	NA	-	Dean *et al.*, 1974
Dominant lethal/ 12 CF1 male mice/dose	0, 5 or 10 mg/kg once, 0, 1 or 2 mg/kg x 5 days orally	NA	-	Dean, 1974
Comet assay/ HepG2 cells	25, 50, 100, 200 or 400 µM	NA	+ all doses	Wu *et al.*, 2010

* Acceptable study to DPR scientists based on FIFRA guidelines.
[a] NA = Not Applicable

Several genotoxicity studies were available in the open literature. Hanna and Dyer (1975) reported that dicrotophos was mutagenic in two *E. coli* strains (WP2 uvrA and WP67), but not in other *E. coli* strains (WP2, CM561, CM571, CM611 and WP12) or in any *S. typhimurium* strains (hisC117, hisG46, TA1530, TA1531, TA1532, TA1534, TA1535, TA1536, TA1537 and TA1538). Also, the increase in the mutagenic response for *E. coli* WP67 was not seen until incubated for 72 hrs compared to the standard 48 hrs. While not specifically mentioned, it does not appear that a metabolic activation step (S-9) was added to the assay. Few details were provided in this report including the concentrations tested, so these results were considered more qualitative and not included in Table 15. Breau *et al.* (1985) reported an increase in mutation frequency with *S. typhimurium* TA100 strain with and without S-9 at the two highest concentrations tested (500 and 5000 µg/plate). No other strains were tested. Nishio and Uyeki (1981) reported an increased in sister chromatid exchanges in Chinese hamster ovary cells exposed to dicrotophos at the two highest concentrations, 0.3 and 1.0 mM. More recently, Wu *et al.* (2010) evaluated the genotoxicity of dicrotophos with three assays, an reverse mutation assay with *S. typhimurium*, an *in vitro* chromosomal aberrations assay with CHO-K1 cells and a comet assay with Hep G2 cells. The mutation frequency was significantly increased in the reverse mutation assay in all strains tested (TA97a, TA98, TA100, TA102, and TA1535) with and without S-9, but only at the highest concentration tested, 5000 µg/plate. An increase in chromosomal aberrations was seen in the CHO-K1 cells at all dose levels tested (0.375 – 1.6 mM) with and without S-9. No cytotoxicity was seen at any concentration in this assay. In addition, DNA damage was seen in the HepG2 cells at all concentrations tested (25 – 400 µM). Dicrotophos was slightly cytotoxic to HepG2 cells at 12 – 200 µM incubated for 24hrs, but not 2 hrs. Therefore, dicrotophos was only incubated for 2 hrs at 400 µM in this assay.

II.C.4. Structure Activity Relationship

Dicrotophos is structurally similar to monocrotophos. The oncogenicity and genotoxicity data submitted to DPR for monocrotophos was reviewed (see Appendix II for DPR's Toxicology Summary for monocrotophos). No increase in tumors was seen in either rats or mice. However, there was some evidence of genotoxicity in the studies submitted, although none met current guidelines. Mutagenicity assays with *S. typhimurium* and other microbes were mostly negative, but a few were positive including a reverse mutation assay with *S. typhimurium* strain TA100 and another forward mutation assay with the mouse lymphoma L5178Y $TK^{+/-}$ cells. Most of the assays for chromosomal damage were negative (including dominant lethal and micronucleus assays), but a sister chromatid exchange assay was positive. Several assays for DNA damage were positive including assays for mitotic gene conversion and mitotic recombination in yeast and unscheduled DNA synthesis in mammalian cells. Pharmacokinetic studies in rats showed that <1 to 3% of dicrotophos is demethylated to monocrotophos after oral dosing.

II.C.5. ToxCast Data

Dicrotophos was tested in various ToxCast assays, although only a few came out positive (Table 16) (U.S. EPA, 2015b). The positive Bioseek (BSK) assays suggest some inflammatory responses are up-regulated. Disruption of immune/inflammatory signaling has been associated with thyroid tumors (Kleinstreuer *et al.*, 2013), but the positive BSK assays for dicrotophos were not ones commonly associated with thyroid tumors in rodents. Disruption of thyroid hormone levels through inhibition of some cytochrome P450 (CYP) enzymes regulated by Pregnane X

receptor (PXR) (e.g., CYP3A4) are also associated with thyroid tumors in rodents (Kleinstreuer *et al.*, 2013). Although not specifically mentioned by Kleinstreuer *et al*. (2013), CYP2C19 is another target gene of PXR, so the positive Novascreen (NVS) assay for this CYP enzyme could be related to the thyroid tumors. The inhibition of human ES (esterase or butyrylcholinesterase - BuChE) in the NVS assay is not surprising since dicrotophos is a ChE inhibitor. The NVS AChE assays were inactive in humans and rats for dicrotophos, but were not included in the ToxCast dashboard, because they were tested at only one concentration (25 µM)[2]. The NVS assays are cell-free assays and include no metabolic activation, but dicrotophos does not require metabolic activation to inhibit AChE. This was also true for the NVS_NR_hTRa assay (not in the Dashboard, but tested at one concentration and inactive). While none of the other ToxCast assays for thyroid hormone receptor were positive, it should be noted that the thyroid pathway has not been fully developed in ToxCast at this time. The one positive Attagene (ATG) assay for the estrogen response element (ERE) is of questionable significance since it's the only assay for the estrogen receptor pathway that was positive. The ERE may be somewhat promiscuous since this assay was positive for a number of chemicals in ToxCast. Also, there was no evidence of estrogenic effects in the *in vivo* studies for dicrotophos.

Table 16. Positive ToxCast Assays for Dicrotophos

Bioseek	Novascreen	Attagene
BSK_KF3CT_MCP1_up BSK_LPS_PGE2_up BSK_SAg_CD38_up	NVS_ADME_hCYP2C19 NVS_ENZ_hES	ATG_ERE_CIS_up

II.C.6. Conclusions

The reduced survival in rats and mice could have affected tumor incidence. ToxCast data suggests that mechanism of action for the thyroid tumors may involve the disruption in inflammatory signaling and inhibition of CYP enzymes which would be threshold mechanisms. Results from the genotoxicity tests for dicrotophos were mixed. Dicrotophos was weakly mutagenic with some bacteria strains in reverse mutation assays where the increase in mutation frequency was not significant until high doses. It was positive in one mouse lymphoma forward mutation assay with L5178Y TK+/- cells. In general, the mouse lymphoma assay does not correlate as well with the rodent cancer bioassays as does the reverse mutation assay with *Salmonella typhimurium* (Tennant *et al.*, 1987; Zeiger *et al.*, 1990). Chromosomal damage was not seen in two *in vivo* assays with mouse bone marrow, but was seen in in CHO cells *in vitro* both as chromosomal aberrations and sister chromatid exchanges. A host-mediated assay and a dominant lethal assay in mice were negative, but a Comet assay with HepG2 cells was positive. Some of the negative assays were older studies that did not meet current guidelines, but some of the positive studies were published studies that often lacked the detail to effectively evaluate

[2] This was determined by comparing two files (AllResults_hitc_Matrix_141121 and AllResults_tested_Matrix_141121) downloaded from ToxCast Summary Files available on USEPA's Interactive Chemical Safety for Sustainability (iCSS) Dashboard (http://www.epa.gov/ncct/toxcast/data.html). For these assays, the "tested" file had "1" for dicrotophos indicating that it had been tested, but "NA" in the "hitc" file indicating that it had not been tested at multiple concentrations. The one concentration tested in all of these assays was 25 µM (Sipes *et al.*, 2013)

study quality. Even if dicrotophos was clearly genotoxic, the weight of evidence for carcinogenicity was still insufficient to perform a quantitative assessment since the increase in tumors was only seen at the high dose in one sex in one species.

II.D. Critical Endpoints and Reference Levels

The critical BMDLs/NOELs selected for evaluating exposures to dicrotophos in this risk assessment are summarized in Table 17. The BMDLs selected for evaluating exposure to dicrotophos in this risk assessment sometimes differed from those selected by U.S. EPA, even when the same study and endpoint were used. This is likely due to the inclusion of the Hill model in the HHAB BMD analysis. A $BMDL_{10}$ of 0.03 mg/kg/day for brain ChEI in PND8 males of was selected as the critical NOEL for evaluating acute oral exposure in the general population which includes children. This $BMDL_{10}$ is the lowest $BMDL_{10}$ for pre-weanling rats of either gender. The critical NOEL selected for evaluating steady-state oral exposure is the $BMDL_{10}$ for brain ChEI in female rats from the subchronic neurotoxicity study observed at weeks 5, 9 and 14 (Horner, 1995). This $BMDL_{10}$ was not as low at that seen in rats administered dicrotophos by gavage for 28 days (Brammer, 2002c), but the bolus dosing in this study may have resulted in artificially greater brain ChEI than would be seen with dietary and drinking water exposures in humans. Children do not appear to be more sensitive than adults with repeated exposure based on the comparative ChE study in neonatal and adult rats exposed for 7 consecutive days (Moxon, 2003b)

The BMDL of 2.1 mg/kg/day for brain ChEI in female rats was selected as the critical NOEL to evaluate dermal exposure to dicrotophos in humans in this risk assessment. The dermal NOEL was adjusted for dermal absorption (estimated 43.7% in rats) and for the difference in exposure duration between rats and humans (6 hrs/8 hrs), resulting in a final absorbed dermal NOEL of 0.69 mg/kg/day which was used for evaluating acute and seasonal exposure of handlers. For bystanders, the human exposure period (1.5 hrs) was shorter than the animal exposure (6 hrs), so there was no adjustment in the dermal NOEL when evaluating their exposure. Consequently, the absorbed dermal NOEL used for bystanders was 0.92 mg/kg/day.

The 28-day inhalation study in rats was selected as the definitive study for evaluating inhalation exposure. In this study the $BMDL_{10}$ values for males and females were similar, so the average value of 0.42 µg/L was used for evaluating inhalation exposure to dicrotophos in humans. HHAB used a default breathing rate for rats of 0.96 m^3/kg/day or 40 L/kg/hr, resulting in an absorbed inhalation NOEL of 0.101 mg/kg/day (0.42µg/L x 6 hr/day x 40 L/kg/hr). HHAB assumed 100% inhalation absorption.

Table 17. Critical Endpoints and NOELs Selected for Evaluating Exposure to Dicrotophos

Exposure Scenarios	BMDL (Internal NOEL)	RfD/RfC (Internal RfD/RfC)	Effects	Ref. [a]
Oral				
Acute	0.03 mg/kg/day	0.0003	↓ Brain ChEI	1
Steady-State	0.025 mg/kg/day	0.00025	↓ Brain ChEI	2*
Dermal				
All durations	2.1 mg/kg/day (0.92 mg/kg/day)	21 µg/kg/day (9.2 µg/kg/day)	↓ Brain ChEI	3
Inhalation				
All durations	0.42 µg/L (0.101 mg/kg/day)	4.2 ng/L (1.01 µg/kg/day)	↓ Brain ChEI	4
Cancer				
All routes	Limited evidence: Increased thyroid tumors in male mice, no tumor increase in female mice or rats of either gender. Results from acceptable genotoxicity tests based on FIFRA guidelines were mixed: negative in reverse mutation assays with *S. typhimurium*, positive in forward mutation with mouse lymphoma assay and negative in micronucleus assay in mouse bone marrow. Evidence was insufficient for a quantitative assessment for cancer.			5* 6* 7* 8* 9*

[a] References: 1. Moxon, 2003a; 2. Horner, 1995;3. Noakes, 2001; 4. Blair, 2010; 5. Milburn, 1998; 6. Allen, 1998; 7. San and Wyman, 1994; 8. San and Clarke, 1995; 9. Putnam and Young, 1994.
* Acceptable study to DPR scientists based on FIFRA guidelines.

III. EXPOSURE ASSESSMENT

III.A. Dietary and Drinking Water Exposure

III.A.1. Residue Data

This assessment used a Tier 2 approach (DPR, 2009) with cottonseed residue data from two residue studies submitted to DPR by the registrant, one on the raw agricultural commodities (undelinted cottonseed and cotton gin byproducts), and another on processed cotton processed products (refined cottonseed oil, meal and hulls). The dicrotophos residue study of cotton raw agricultural commodities (RAC) included twelve test sites in Arkansas (1), California (3), Georgia (1), Louisiana (1), Mississippi (1), New Mexico (1), Oklahoma (1), and Texas (3) (Prochaska, 1998a). Each treated plot received 3 applications of Bidrin 8® at target label rates of 0.25 lb AI/acre for early season and 0.50 lb AI/acre for mid and late season. The cotton was harvested 30 days after the last application. Duplicate samples of undelinted cottonseed were analyzed per site. The highest residue detected in all 12 sites was 0.074 ppm for one sample from New Mexico. The average residue for all 12 sites was 0.027 ppm using a limit of detection (LOD) of 0.01 ppm for samples with no detectable residues. It should be noted that the drier states such as California, New Mexico, Oklahoma and Texas tended to have the higher residue levels. Samples from the one site in southeast Texas with higher rainfall had no detectable residues compared to samples from the other two sites in northwest Texas. The average residue for samples from these by drier sites (excluding southeast Texas site) was 0.040 ppm. For California sites, the highest residue was 0.048 ppm and the average was 0.032 ppm. This study also measured the dicrotophos residues in cotton gin byproducts. By comparison the highest

residue in cotton gin byproducts was 1.53 ppm and the average residue was 0.488 ppm. These residues are nearly 20 times higher than for undelinted cottonseed.

The residue study of cotton processed commodities was conducted in southeast Texas (Prochaska, 1998b). The test site consisted of one control plot and two treated plots, each was 4380 sq ft., with a buffer of 797 ft. between control and treated plots and 20 ft. between treated plots. One of the treated plots was treated at the maximum label rate with one early season application at 0.26 lb AI/acre and two applications in mid and late season at 0.51 lb AI/acre. The other treated plot was treated at a 5X exaggerated rate (one early season application at 1.23 lb AI/acre application and a mid and late season application at 2.52 lb AI/acre). No dicrotophos residues were detected in the undelinted cottonseed, hulls, meal or refined cottonseed oil at the maximum label rate. The limit of detection (LOD) was 0.01 ppm. Even at the exaggerated rate, no residues were detected in the refined cottonseed oil or meal, but it was detected at 0.0189 and 0.0113 ppm in the cottonseed hulls and undelinted cottonseed, respectively. These results suggest that the residues in the undelinted cottonseed are primarily in the hulls and lint, not the meal or oil. Since only one test site was used in this study which was a site with higher rainfall than California and only one refined cottonseed oil sample was analyzed, this study was not selected for use in this dietary assessment. For this reason, the residue values in undelinted cottonseed from the cotton RAC study was selected for use in the dietary exposure even though these residue values most likely exaggerates the residues found in refined cottonseed oil. Only the residue values from the drier sites were used since higher rainfall appears to significantly reduce the residues. The average value from these drier sites (0.040 ppm) was used for both acute and steady-state exposure because cottonseed oil is considered a blended product.

Finished drinking water samples for dicrotophos from PDP's 2008-2013 monitoring were selected for estimating drinking water exposure. Older data was not used because the LOD was much higher (132 ppt). The LODs for the more recent samples were between 0.9 and 9.0 ppt. The PDP data was also limited to the southern states which grow cotton. California was not included even though it grows cotton because dicrotophos was not registered for use in California during this time. Therefore, only 400 samples were used in this drinking water assessment from the following states: Texas (11), Louisiana (71), Missouri (32), Tennessee (70), Kentucky (29), Georgia (46), North Carolina (69) and Virginia (71). Only 4 samples from North Carolina in 2012 had detectable residues between 1.5 and 3.4 ppt which were just above the LOD for that lab (0.9 ppt).

III.A.2. Software

The acute and steady state dietary and drinking water exposure analyses were conducted using the Dietary Exposure Evaluation Model (DEEM-FCID™, version 4.02) software program developed by Durango Software, LLC, which utilizes food translations based on EPA/USDA FCID recipe set as of August 2014. The Acute Analysis program estimates the distribution of exposure per capita and per user-day (i.e., the percentile exposure for only individuals that consume on that survey day at least one commodity on which the pesticide of concern is used). However, since both cottonseed oil and water are consumed by most people, there was not much difference in the per capita and per user-day exposure estimates. The Acute Analysis program was used for both acute and steady state exposure, but for steady state exposure the 2-day

average consumption and mean estimates per user were selected. Due to the limited residue data for cottonseed oil residues, a deterministic approach was used. Due to the large number of samples available for drinking water a probabilistic approach or Monte Carlo method was used where residue and consumption values are randomly selected from different distribution curves. DEEM-FCID™ uses the 2-day consumption data from the National Health and Nutrition Examination Survey (NHANES) from 2005-2010. These data provide information on 2-day food intake by 24,673 individuals of all ages including 1,190 infants, 1,479 children 1-2 years old, 1,418 children 3-5 years old, 3,316 children 6-12 years old and 3,486 youths 13-19 years old.

III.A.3. Exposure Estimates

In the Acute Analysis program in DEEM-FCID, the 2-day consumption for each person can be treated as a separate event (i.e., unrelated) or it can be averaged. For acute exposure estimates, the 2 days of consumption were treated as separate events and an upper percentile of exposure was selected depending on whether a deterministic approach (95th percentile) or probabilistic approach (99.9th percentile) was used. If a combination of point estimates (deterministic) and distributions (probabilistic) were used for different commodities, then an intermediate percentile of 97.5 percentile is used. For dicrotophos food-only exposure estimates, the 95th percentile among users was reported since a point estimate was used for the cottonseed oil residue. For acute drinking water-only exposure, the 99.9th percentile for users was reported since a residue distribution was generated from a residue file with PDP data from 400 finished drinking water samples (i.e., a probabilistic approach was used). When dietary and drinking water exposures were combined, then the 97.5th percentile was selected since the residue file consisted of point estimates and distributions. For steady-state exposures, the Acute Analysis was run again with the same residue file, but the 2-day consumption was averaged and the mean consumption per users for each population subgroup was reported.

The results of the acute and steady state dietary analysis are shown in Table 18. The detailed reports from DEEM-FCID are in Appendix IV. Since point estimates of residue levels were used for the dietary exposure with the Tier 2 analysis, the 95th percentile and mean exposure estimates among users were selected for evaluating acute and steady state dietary exposure, respectively. The acute dietary exposure estimates ranged from 2.11 ng/kg/day for adults 18+ years old to 7.01 ng/kg/day for children 1-2 years old. The steady state dietary exposure estimates were about a third of the acute exposures, ranging from 0.54 ng/kg/day for nursing infants less than 1 year old to 2.73 ng/kg/day for children 3-5 years old.

The results of the acute and steady state drinking water analysis are also shown in Table 18 (see Appendix IV for detailed DEEM-FCID report). Since a probabilistic approach was used with this residue data, the 99.9th percentile and mean exposure estimates for users were selected for the evaluating the acute and steady state drinking water exposure, respectively. The acute estimates ranged from 0.81 ng/kg/day for females 13-49 years old to 2.65 ng/kg/day for non-nursing infants less than one year old. The steady state exposure estimates were much lower, ranging from 0.09 ng/kg/day for children 6-12 years old to 0.53 ng/kg/day for non-nursing infants less than one year old.

Table 18. Dietary and Drinking Water Exposure Estimates

Population Subgroup	Dietary ng/kg/day		Drinking Water ng/kg/day		Combined Exposure ng/kg/day	
	Acute 95th percentile	Steady-State mean	Acute 99.9th percentile	Steady State mean	Acute 97.5th percentile	Steady State mean
U.S. Population	3.19	1.04	1.17	0.11	4.51	1.13
Nursing infants < 1 yr	2.95	0.54	2.18	0.19	3.05	0.43
Non-nursing infants < 1 yr	4.04	0.82	2.65	0.53	3.50	0.91
All infants < 1 yr	3.69	0.76	2.63	0.45	3.38	0.80
Children 1-2 yrs	7.01	2.49	1.69	0.15	9.13	2.62
Children 3-5 yrs	6.70	2.73	1.07	0.12	8.76	2.85
Children 6-12 yrs	5.21	1.97	0.92	0.09	6.95	2.06
Females 13-49 yrs	2.24	0.81	0.81	0.11	3.22	0.91
Adults 18+ yrs	2.11	0.76	0.78	0.10	2.91	0.86

The 97.5th percentile for users is selected to determine the acute exposure when dietary and drinking water residues were combined in the same assessment and both point estimates and distributions are used for the residues (Table 18 and Appendix IV). The mean estimate is still used for evaluating the steady-state exposure. Due to changes in the user population when commodities are added, sometimes the combined exposure for users can be less than the individual commodity exposure for users. An example of this can be seen with non-nursing infants who have higher acute dietary exposures. The reason being is that because only 38.4% are users compared to the combined dietary and drinking water exposure for this population subgroup in which 97.8% are users. Consequently, the acute dietary exposure for non-nursing infants at the 95th percentile is higher (4.04 ng/kg/day) than the combined dietary and drinking water exposure at the 97.5th percentile (3.50 ng/kg/day). The acute combined exposure estimates ranged from 2.91 ng/kg/day for adults 18+ years old to 9.13 ng/kg/day for children 1-2 years old. The steady state combined exposure estimates were about one-third of the acute combined exposure ranging from 0.43 ng/kg/day for nursing infants less than 1 year old to 2.85 ng/kg/day for children 3-5 years old.

III.B. Handler Exposure

The exposure estimates for dicrotophos with use on cotton are described in detail in a separate exposure assessment document (EAD) in Appendix V. Only a brief summary of these estimates is included here. The dermal and inhalation exposure dosages, short-term absorbed daily dosage (STADD) and seasonal absorbed daily dosage (SADD), for handlers are summarized in Tables 4-6 in the EAD (Appendix V). For handlers, the dermal STADDs ranged from 0.00961

mg/kg/day for scouts to 0.215 mg/kg/day for flaggers with aerial application. The dermal SADDs were between 0.000573 and 0.0771 mg/kg/day with scouts having the lowest and flaggers having the highest exposures. The inhalation STADDs for handlers were much lower than the dermal STADDs, ranging from 0.000208 mg/kg/day for ground boom applicators to 0.00379 mg/kg/day for aerial mixer/loaders. The inhalation SADDs for handlers were between 0.0000746 and 0.00135 mg/kg/day with ground boom applicators having the lowest and aerial mixer/loaders having the highest.

III.C. Bystander Exposure

III.C.1. Adults

Drift deposition exposure (in µg/kg/day) and inhalation exposure estimates (1 hour time-weighted average air concentrations in µg/kg/day) for adults are shown in Table 7 in the EAD (Appendix V). Exposures were estimated for aerial application at various distances from a treated field (25-1,000 ft.) using the AGDISP model with two different application rates (0.25 and 0.5 lb AI/acre) and two different types of aircraft (fixed wing AT 802A and Bell 205 helicopter). Adult bystander dermal exposure was also estimated for ground boom application using the AgDRIFT model with two different rates (0.025 and 0.5 lb AI/acre) and high and low boom equipment, but the distances from the field were shorter (25-250 ft). The AgDRIFT ground boom model does not have the capability to produce air concentrations so there is no estimate of inhalation exposure for ground boom equipment. At 25 ft. from the treated field, the adult bystander acute dermal exposure ranged from 0.550 µg/kg/day with ground boom application at 0.25 lb AI/acre using a low boom to 11.25 µg/kg/day with aerial application at 0.5 lb AI/acre using a Bell 205 helicopter. With aerial application, the adult bystander inhalation exposure at 25 ft from the treated field ranged from 2.78 µg/kg/day with a fixed wing AT 802A aircraft to 5.52 µg/kg/day with a Bell 205 helicopter at 0.5 lb AI/acre.

III.C.2. Children

Acute oral, dermal, and inhalation exposures from dicrotophos spray drift were estimated for child bystanders using two different aerial application rates (0.25 and 0.5 lb AI/acre) and two different types of aircraft (fixed wing AT 802A and Bell 205 helicopter) at various distances from the treated field (25-1,000 ft). These values are shown in Table 8 in EAD (Appendix V). Oral exposure from drift for 3 separate activities (hand to mouth, object to mouth, and soil ingestion) were combined. As a result, 24 exposure estimates were calculated at each distance including total oral exposure. The same combination of exposures were also estimated for child bystanders for ground boom using two different application rates and two different boom heights at various distances from the treated field (25-250 ft). These values are shown in Table 9 in the EAD (Appendix V). As with adults, inhalation exposure could not be calculated for child bystanders with ground boom application because the AgDRIFT ground boom model does not have the capability to produce air concentration estimates. Therefore, only 20 oral and dermal exposure estimates were calculated for ground boom application at distances of 25-250 ft from the treated field. As with adult bystanders, the exposures were consistently lower with ground boom application compared to aerial application for each activity.

Regardless of application method, oral exposures with the lowest estimates at 25 ft were soil ingestion, ranging from 0.00006 µg/kg/day with ground boom application using a low boom at a rate of 0.25 lb AI/acre to 0.0028 µg/kg/day with aerial application using a fixed wing aircraft at an application rate of 0.5 lb AI/acre. Hand to mouth activity resulted in the highest estimates at 25 ft, ranging from 0.029 µg/kg/day with ground boom application using a low boom at 0.25 lb AI/acre to 1.28 µg/kg/day with aerial application using a fixed wing aircraft at 0.5 lb AI/acre. The absorbed dermal exposure estimates were much higher than most of the oral exposures ranging from 0.368 to 16.5 µg/kg/day at 25 ft. from the field edge. The inhalation exposures with aerial application were also high, ranging from 6.96 µg/kg/day when applied with a fixed wing aircraft at 0.25 lb AI/acre to 14.4 µg/kg/day when applied with a helicopter at rate of 0.5 lb AI/acre. Exposure estimates were fairly similar between types of aircraft used in aerial application at the same application rate and distance.

III.D. Aggregate Exposure

The dietary and drinking water exposures in Table 18 were aggregated with the occupational and bystander exposures from Tables 4-9 in the EAD (Appendix V). It was assumed that handlers consumed 2.91 dicrotophos through diet and 0.86 ng/mg/day through drinking water combined for acute and steady-state exposure based on the custom population of adults 18+yrs old, as shown at the bottom of Table 18. The aggregate MOEs for handlers are summarized in Table 19. For handlers, the dietary and drinking water exposure represented less than 0.1% of their total exposure. The exception was cotton scouts, whose lowest combined seasonal exposure to dicrotophos residue in diet and drinking represented almost 0.3% of their total exposure.

Table 19. Aggregate Exposures for Handlers

Scenario	Acute		Seasonal	
	Total Exposure [a] (mg/kg/day)	% Total Exposure Diet+Water	Total Exposure (mg/kg/day)	% Total Exposure Diet+Water
Aerial Application				
Mixer/loaders	0.119	0.002	0.043	0.002
Applicators	0.091	0.003	0.033	0.003
Flaggers	0.216	0.001	0.078	0.001
Ground Application				
Mixer/loaders	0.020	0.015	0.007	0.012
Applicators	0.008	0.036	0.003	0.030
Post-application				
Scouts	0.005	0.058	0.0003	0.292

[a] Dermal and inhalation exposure dosages are from Tables 4-6 in the EAD for dicrotophos (Appendix V). Dietary and drinking water exposure was assumed to 2.912 and 0.86 ng/kg/day for acute and seasonal/steady-state exposure for workers, 18+ years old, respectively (refer to values in Table 18).

The aggregate exposure for adult and child bystanders is summarized in Table 20. It was assumed that the combined dietary and drinking water exposure for adult and child bystanders was 2.91 and 9.13 ng/kg/day, respectively, based on the estimated exposure for adults 18+ yrs old and children 1-2 yrs old (see Table 18). For adult bystanders, the dietary and drinking water

contribution to total exposure ranged from less than 0.2% with aerial application to almost 3% with ground boom application because the drift exposure was lower. For child bystanders, the dietary and drinking water contribution to total exposure was approximately 3 times higher than adults, especially with ground application where drift exposure was lower.

Table 20. Aggregate Exposure for Adult and Child Bystanders [a]

Rate	Equipment	Adult		Children	
		Total Exposure (µg/kg/day)	% Total Exposure Diet+Water	Total Exposure (µg/kg/day)	% Total Exposure Diet+Water
Aerial Application at 1000 ft.					
0.25 lb/A	**Fixed wing**	1.85	0.16	4.01	0.23
	Helicopter	1.61	0.18	3.54	0.26
0.50 lb/A	**Fixed wing**	2.96	0.10	6.20	0.15
	Helicopter	2.42	0.12	5.18	0.18
Ground Application at 250 ft.					
0.25 lb/A	**Fixed wing**	0.24	1.21	0.30	3.04
	Helicopter	0.11	2.65	0.09	10.19
0.50 lb/A	**Fixed wing**	0.48	0.61	0.59	1.54
	Helicopter	0.22	1.34	0.17	5.36

[a] Dermal and inhalation exposure dosages are from Tables 7-9 in the EAD for dicrotophos (Appendix V). Combined dietary and drinking water exposure was assumed to be 2.91 and 9.13 ng/kg/day for adults and children (1-2 yrs old), respectively (Table 18).

IV. RISK CHARACTERIZATION

The risk for non-carcinogenic human health effects is expressed as a margin of exposure (MOE). The MOE is the ratio of the NOEL or BMDL from experimental animal studies to the human exposure dosage.

$$MOE = \frac{NOEL}{Exposure\ Dosage}$$

When exposure occurs by more than one route and route-specific NOELs are used, a combined MOE for all routes can be calculated. This is similar to the way a Hazard Index is calculated by taking the inverse of the sum of the inverses of the MOEs for each route, provided that NOELs for the same or related endpoints were used to calculate the MOE for each route.

$$MOE_{combined} = \frac{1}{\frac{1}{MOE_{oral}} + \frac{1}{MOE_{dermal}} + \frac{1}{MOE_{inhalation}}}$$

IV.A. Diet and Drinking Water

The MOEs for dietary and drinking water exposures in various population subgroups are summarized in Table 21. The acute dietary and drinking water MOEs were calculated used a $BMDL_{10}$ of 0.03 mg/kg/day based on brain ChEI in PND8 male rat pups (Moxon, 2003a). The

steady-state dietary and drinking water MOEs were calculated using a $BMDL_{10}$ of 0.025 mg/kg/day based on brain ChEI in female rats from the subchronic neurotoxicity study which was observed at weeks 5, 9, and 14 (Horner, 1995). The exposure dosages for dietary and drinking water exposure are from Table 18. The MOEs for dietary and drinking water exposure were all greater than 1,000 for all population subgroups when considered alone or combined with either acute or steady state exposure.

Table 21. Margins of Exposure for Dietary and Drinking Water Exposure

Population Subgroup	Dietary MOE [a]		Drinking Water MOE		Combined MOE	
	Acute	Steady State	Acute	Steady State	Acute	Steady State
U.S. Population	9,400	24,000	26,000	230,000	6,600	22,000
Nursing infants < 1 yr	10,000	46,000	14,000	130,000	9,800	59,000
Non-nursing infants < 1 yr	7,400	31,000	11,000	47,000	8,600	27,000
All infants < 1 yr	8,100	33,000	11,000	55,000	8,900	31,000
Children 1-2 yrs	4,300	10,000	18,000	170,000	3,300	9,500
Children 3-5 yrs	4,500	9,200	28,000	210,000	3,400	8,800
Children 6-12 yrs	5,800	13,000	33,000	280,000	4,300	12,000
Females 13-49 yrs	14,000	31,000	37,000	240,000	9,300	28,000
Adults 18+ yrs	14,000	33,000	38,000	240,000	10,000	29,000

[a] MOE = Margin of Exposure = NOEL or BMDL/Exposure. Acute MOEs calculated using $BMDL_{10}$ of 0.03 mg/kg/day based on brain ChE inhibition in PND8 rat pups (Moxon, 2003a). Steady state MOEs calculated using $BMDL_{10}$ of 0.025 mg/kg/day based on brain ChEI in female rats in a subchronic neurotoxicity study (Horner, 1995). Exposure dosages are from Table 18 in the Exposure Assessment section of this document.

IV.B. Handlers

Table 22 summarizes the MOEs for dermal and inhalation exposure in handlers involved in the application of dicrotophos to cotton. The MOEs for systemic effects from dermal exposure were calculated using the $BMDL_{10}$ of 2.1 mg/kg/day based on brain ChE inhibition in female rats in 28-day dermal study (Noakes, 2001). Assuming a rat dermal absorption of 43.7% (Ngo, 2015) and adjusting for the 6 hrs/day exposure in rats versus the 8-hrs/day exposure in workers, the absorbed dermal NOEL was 0.69 mg/kg/day. This one subchronic dermal NOEL was used for evaluating both short-term and seasonal dermal exposure for handlers to dicrotophos. The dermal exposure dosages for handlers are in Tables 4-6 in the EAD for dicrotophos (Appendix V). The MOEs for dermal exposure were all less than 100, except for seasonal exposure for ground boom mixer/loaders and applicators and scouts.

Table 22. Margins of Exposure for Handlers Involved in Application of Dicrotophos to Cotton

	Dermal MOE [a,b]		Inhalation MOE [a,c]		Combined MOE	
	Short-term	Seasonal	Short-term	Seasonal	Short-term	Seasonal
Aerial Application						
Mixer/Loaders	6	17	27	75	5	14
Applicators	8	21	130	360	8	20
Flaggers	3	9	59	160	3	9
Ground Application						
Mixer/Loaders	36	100	160	450	29	82
Applicators	88	250	490	1,400	75	210
Post-application						
Scouts	137	2,300	NC	NC	137	2,300

[a] MOE = Margin of Exposure = NOEL or BMDL/Exposure. Combined MOE = $1/(1/MOE_{dermal}+1/MOE_{inhalation})$. MOEs were rounded to two significant figures. Exposure dosages are from Tables 4-6 in the EAD for dicrotophos (Appendix V).
[b] $BMDL_{10}$ = 2.1 mg/kg/day based on brain ChE inhibition in female rats in 28-day dermal study (Noakes, 2001). Assuming a rat dermal absorption of 43.7% and adjusting for 6 hr exposure in rats (Ngo, 2015) versus 8-hr exposure in workers, the absorbed dermal NOEL = 0.69 mg/kg/day.
[c] $BMDL_{10}$ = 0.42 µg/L based on brain ChE inhibition in male and female rats in 28-day inhalation study (Blair, 2010). Assuming a rat breathes 40 L/kg/hr and rats were exposed 6 hrs, the absorbed inhalation NOEL is 0.101 mg/kg/day.
NC = Not calculated

The MOEs for systemic effects with inhalation exposure were calculated using the $BMDL_{10}$ of 0.42 µg/L for brain ChE inhibition in male and female rats in the 28-day inhalation study (Blair, 2010). Assuming 100% absorption by the inhalation route and a breathing rate for rats of 40 L/hr for 6 hrs, the absorbed inhalation NOEL is 0.101 mg/kg/day. This inhalation NOEL was used for evaluating both short-term and seasonal inhalation exposure to dicrotophos. The inhalation exposure dosages for handlers are also found in Tables 4-6 in the EAD (Appendix V). Unlike dermal exposure, the inhalation MOEs were almost all over 100, except for mixer/loaders (short-term and seasonal) and flaggers (short-term) with aerial application. The combined dermal and inhalation MOEs are similar to the dermal MOEs for the same scenarios since most of the exposure is coming by the dermal route.

IV.C. Bystanders

IV.C.1. Adults

The MOEs for acute dermal exposure to dicrotophos from cotton spray drift in adult bystanders is summarized in Table 23. The $BMDL_{10}$ for brain ChEI from the 28-day dermal ChE study by Noakes (2001) was used and adjusted for a rat dermal absorption of 43.7%. No adjustment was made for differences in exposure between animals and humans since it was assumed humans were exposed for less time (1.5 hrs/day) than animals (6 hrs/day). Consequently, the absorbed dermal NOEL used to calculate the MOEs for adult bystanders was higher (0.92 mg/kg/day) than for handlers (0.69 mg/kg/day). The estimated dermal exposure dosages for adult bystanders are from Table 7 in the EAD (Appendix V). The dermal MOEs for adult bystanders were greater

than 100 at 25 ft. for all ground boom application scenarios and at 25-50 ft. for the aerial application scenarios depending on application rate.

The MOEs for acute inhalation exposure to dicrotophos cotton spray drift in adult bystanders with aerial application are also summarized in Table 23. As mentioned in the exposure section, no inhalation MOEs were calculated for adult bystanders with ground boom application since the AgDRIFT ground boom model does not have the capability to provide air concentration values necessary to estimate inhalation exposure with this application method. The inhalation MOEs were calculated using the $BMDL_{10}$ of 0.42 µg/L for brain ChE inhibition in male and female rats in the 28-day inhalation study (Blair, 2010). Assuming 100% absorption by the inhalation route and a breathing rate for rats of 40 L/hr for 6 hrs, the absorbed inhalation NOEL is 0.101 mg/kg/day. The inhalation exposure dosages for adult bystanders with aerial application are also in Tables 7 in the EAD. Unlike dermal exposure, the inhalation MOEs with aerial application were all less 100, except at 1,000 ft from the field edge with helicopter application at 0.25 lb AI/acre. The combined dermal and inhalation MOEs are more similar to the inhalation MOEs even though the dermal exposure was greater because the inhalation NOEL was lower (0.101 mg/kg/day vs 0.92 mg/kg/day).

IV.C.2. Children

Evaluation of acute exposure to dicrotophos from spray drift for children was a combination of dermal, inhalation, and non-dietary oral exposure. The oral exposures for children were evaluated using the $BMDL_{10}$ of 0.03 mg/kg/day based on brain ChEI in PND8 rats after a single oral dose (gavage) (Moxon, 2003a). The estimated oral exposure for child bystanders is from Table 8 in the EAD (Appendix V). With aerial application, the oral MOEs for child bystanders were greater than 100 at 25 ft. from the field edge. The exception was hand-to-mouth exposures, which were greater than 100 at 250-500 ft. depending on the application rate (Table 24). With ground boom application, the oral MOEs were greater than 100 except with the high boom at 0.5 lb AI/acre, which had an MOE of 94.

Dermal exposure was evaluated using the $BMDL_{10}$ from the 28-day dermal toxicity study in young adult rats (Noakes, 2001). As with adult bystanders, the $BMDL_{10}$ was adjusted for dermal absorption, but not for differences in exposure between animals and humans since humans were exposed for less time than animals. So the same absorbed dermal NOEL used to calculate the MOEs for adult bystanders was used for child bystanders. The dermal exposure dosages are from Table 8 in the EAD (Appendix V). The dermal MOEs for child bystanders with aerial application were greater than 100 at 25 ft. when applied at 0.25 lb AI/acre, but were not greater than 100 until 100 ft from the field edge when applied at 0.5 lb AI/acre (Table 24). With ground boom application, the dermal MOEs were all greater than 100 at 25 ft. The inhalation MOEs for child bystanders were calculated using the $BMDL_{10}$ of 0.42 µg/L for brain ChE inhibition in male and female rats in the 28-day inhalation study (Blair, 2010).

Table 23. Margins of Exposure for Acute Exposure in Adult Bystanders to Dicrotophos Cotton Spray Drift

Application method	Application Rate	Equipment	Exposure route	Margin of Exposure [a]					
				25ft	50 ft	100 ft	250 ft	500 ft	1000 ft
Aerial	0.25 lb AI/acre	Fixed wing AT 802A	Dermal	170	210	310	580	880	1,200
			Inhalation	36	39	44	55	67	92
			Combined MOE	30	33	38	50	62	86
		Bell 205 Helicopter	Dermal	170	280	460	650	900	1,500
			Inhalation	32	36	42	53	69	100
			Combined MOE	27	32	39	49	64	95
	0.5 lb AI/acre	Fixed wing AT 802A	Dermal	83	100	150	270	430	640
			Inhalation	21	23	26	33	43	66
			Combined MOE	17	19	22	29	39	60
		Bell 205 Helicopter	Dermal	82	1303	210	310	470	870
			Inhalation	18	21	25	33	47	74
			Combined MOE	15	18	22	30	43	68
Application method	Application Rate	Equipment	Exposure route	Margin of Exposure [a]					
				50 ft	75 ft	100 ft	150 ft	200 ft	250 ft
Ground boom	0.25 lb AI/acre	High boom	Dermal	580	940	1,600	2,300	3,100	3,900
		Low boom	Dermal	1,700	2,600	4,100	5,600	7,100	8,600
	0.5 lb AI/acre	High boom	Dermal	290	470	810	1,200	1,500	1,900
		Low boom	Dermal	830	1,300	2,100	2,800	3,500	4,300

[a] Margin of Exposure = NOEL or BMDL/Exposure. The BMDL10 of 2.1 mg/kg/day was used to evaluate dermal exposure based on brain ChE inhibition in female rats in 28-day dermal study (Noakes, 2001). MOE was calculated using the absorbed dermal NOEL of 918 µg/kg/day which assumed a dermal absorption of 43.7% for the rat (Ngo, 2015). No adjustment was made for exposure period since the human exposure (1.5 hrs) was less than the animal exposure (6 hrs). The BMDL10 of 0.42 µg/L was used to evaluate inhalation exposure based on brain ChE inhibition in male and female rats in 28-day inhalation study (Blair, 2010). Assuming rats breathe 40 L/kg/hr and they were exposed 6 hrs, the inhalation NOEL = 101 µg/kg/day.

Table 24. Margins of Exposure for Acute Exposure in Child Bystanders to Dicrotophos Cotton Spray Drift

Application method	Application Rate	Equipment	Exposure route	Margins of Exposure [a]					
				25ft	50 ft	100 ft	250 ft	500 ft	1000 ft
Aerial	0.25 lb AI/acre	Fixed wing AT 802A	Hand to mouth	48	60	86	160	250	340
			Object to mouth	1,600	2,000	2,800	5,400	8,100	11,000
			Soil ingestion	21,000	27,000	37,000	75,000	100,000	150,000
			Oral Total	47	58	83	160	240	330
			Dermal	120	140	210	400	600	830
			Inhalation	14	16	18	22	26	36
			Combined MOE	10	12	14	18	23	31
		Bell 205 Helicopter	Hand to mouth	48	79	130	180	250	420
			Object to mouth	1,500	2,600	4,200	6,000	8,300	14,000
			Soil ingestion	21,000	37,000	60,000	75,000	100,000	150,000
			Oral Total	46	76	130	180	250	400
			Dermal	110	190	310	440	620	1,000
			Inhalation	12	14	16	20	27	40
			Combined MOE	9	11	14	17	23	35
	0.5 lb AI/acre	Fixed wing AT 802A	Hand to mouth	23	29	41	77	120	180
			Object to mouth	760	940	1,300	2,500	4,000	5,900
			Soil ingestion	11,000	13,000	19,000	33,000	60,000	75,000
			Oral Total	23	28	40	74	120	170
			Dermal	57	70	100	190	290	440
			Inhalation	8	9	10	13	17	26
			Combined MOE	5	6	7	10	14	22
		Bell 205 Helicopter	Hand to mouth	23	38	60	87	130	240
			Object to mouth	750	1,200	2,000	2,900	4,300	7,900
			Soil ingestion	10,000	17,000	27,000	37,000	60,000	100,000
			Oral Total	22	36	58	85	130	240
			Dermal	56	91	150	210	320	590
			Inhalation	7	8	10	13	18	29
			Combined MOE	5	6	8	11	15	25

Table 24 (cont.). Margins of Exposure for Acute Exposure in Child Bystanders to Dicrotophos Cotton Spray Drift

Application method	Application Rate	Equipment	Exposure route	Margins of Exposure[a]					
				25 ft	50 ft	100 ft	150 ft	200 ft	250 ft
Ground boom	0.25 lb AI/acre	High boom	Hand to mouth	190	310	540	800	1,100	1,400
			Object to mouth	6,100	10,000	18,000	26,000	35,000	46,000
			Soil ingestion	86,000	140,000	250,000	370,000	500,000	600,000
			Oral Total	180	300	530	770	1,000	1,400
			Dermal	460	750	1,300	1,900	2,600	3,400
			Combined MOE	130	210	380	550	750	980
		Low boom	Hand to mouth	1,000	1,600	2,500	3,300	4,200	5,100
			Object to mouth	34,000	51,000	81,000	110,000	140,000	170,000
			Soil ingestion	500,000	750,000	1,000,000	1,500,000	1,500,000	3,000,000
			Oral Total	1,000	1,500	2,400	3,200	4,000	4,900
			Dermal	2,500	3,800	6,000	7,900	11,000	12,000
			Combined MOE	710	1,100	1,700	2,300	2,900	3,500
	0.5 lb AI/acre	High boom	Hand to mouth	94	150	270	400	540	710
			Object to mouth	3,100	5,000	8,800	13,000	18,000	23,000
			Soil ingestion	43,000	70,000	120,000	190,000	250,000	330,000
			Oral Total	91	150	260	390	520	680
			Dermal	230	370	660	970	1,300	1,700
			Combined MOE	65	110	190	280	370	490
		Low boom	Hand to mouth	510	780	1,200	1,600	2,100	2,500
			Object to mouth	17,000	25,000	41,000	54,000	68,000	83,000
			Soil ingestion	230,000	370,000	600,000	750,000	1,000,000	1,000,000
			Oral Total	500	750	1,200	1,600	2,000	2,500
			Dermal	1,200	1,900	3,000	4,000	5,00	6,200
			Combined MOE	360	540	860	1,100	1,400	1,800

[a] Margin of Exposure = NOEL or BMDL/Exposure. The BMDL10 of 30 µg/kg/day was selected to evaluate the oral exposure for children based on brain ChE inhibition in rats after a single oral dose (gavage). The BMDL10 of 2.1 mg/kg/day was used to evaluate dermal exposure based on brain ChE inhibition in female rats in 28-day dermal study. MOE was calculated using the absorbed dermal NOEL of 918 µg/kg/day which assumed a dermal absorption of 43.7% for the rat (Ngo, 2015). No adjustment was made for exposure period since the human exposure (1.5 hrs) was less than the animal exposure (6 hrs). The BMDL10 of 0.42 µg/L was used to evaluate inhalation exposure based on brain ChE inhibition in male and female rats in 28-day inhalation study. Assuming rats breathe 40 L/kg/hr and they were exposed 6 hrs, the inhalation NOEL = 101 µg/kg/day.

Assuming 100% absorption by the inhalation route and a breathing rate for rats of 40 L/hr for 6 hrs, the absorbed inhalation NOEL is 0.101 mg/kg/day. The inhalation exposure dosages for child bystanders with aerial application are also in Tables 8 in the EAD. The inhalation MOEs for child bystanders with aerial application were lower than MOEs for other routes of exposure for the same scenario and were less than 100 for all scenarios even at 1,000 ft. from the field (Table 24). The combined MOEs for child bystanders were less than 100 for aerial application scenarios because of the inhalation exposure. With ground boom application, the combined MOEs were greater than 100 at 25 ft except when using the high boom at 0.5 lb AI/acre, which were greater than 100 at 50 ft. from the field edge.

IV.C.3. Aggregate Exposure

The aggregate exposure for handlers from acute and seasonal occupational, dietary, and drinking water exposures are summarized in Table 25. The dietary and drinking water exposure represented a very small amount of the total exposure for workers. Consequently, their combined MOEs for total exposure were not significantly different from the combined MOEs from occupational exposure alone. Even when the combined MOE for occupational exposure was greater than 1,000 (e.g., seasonal exposure for scouts), the combined MOE for total exposure was not significantly lower.

Table 25. Aggregate Margins of Exposure for Handlers

	Acute			Seasonal		
Scenario	**Combined MOE [a] Occupation**	**Combined MOE Diet+Water**	**Combined MOE Total**	**Combined MOE Occupation**	**Combined MOE Diet+Water**	**Combined MOE Total**
Aerial Application						
Mixer/loaders	5	10,000	5	14	28,000	14
Applicators	8	10,000	8	21	28,000	20
Flaggers	3	10,300	3	9	28,000	9
Ground Application						
Mixer/loaders	29	10,000	29	82	28,000	82
Applicators	75	10,000	74	210	28,000	210
Post-application						
Scouts	140	10,000	130	2,300	28,000	2,100

[a] MOE = Margin of Exposure = NOEL or BMDL/Exposure. Combined MOE = $1/(1/MOE_{dermal}+1/MOE_{inhalation})$. MOEs were rounded to two significant figures. The $BMDL_{10}$ for dermal exposure is 2.1 mg/kg/day based on brain ChE inhibition in female rats in 28-day dermal study (Noakes, 2001). Assuming a rat dermal absorption of 43.7% and adjusting for 6 hr exposure in rats (Ngo, 2015) versus 8-hr exposure in workers, the absorbed dermal NOEL = 0.69 mg/kg/day. The $BMDL_{10}$ for inhalation exposure is 0.42 µg/L based on brain ChE inhibition in male and female rats in 28-day inhalation study (Blair, 2010). Assuming a rat breathes 40 L/kg/hr and rats were exposed 6 hrs, the absorbed inhalation NOEL is 0.101 mg/kg/day. The $BMDL_{10}$ for oral acute exposure is $BMDL_{10}$ is 0.03 mg/kg/day based on brain ChE inhibition in PND8 rat pups (Moxon, 2003a). The $BMDL_{10}$ for seasonal/steady-state exposure is 0.025 mg/kg/day based on brain ChEI in female rats in a subchronic neurotoxicity study (Horner, 1995). Occupational exposure dosages are from Tables 4-6 in the EAD for dicrotophos (Appendix V). Dietary and drinking water exposure dosages are from Table 18 in this RCD.

The aggregate exposures for adult and child bystanders from acute drift, dietary and drinking water exposure are shown in Table 26. Only the bystander exposures at the maximum distance evaluated were included in this table. At this distance, the drift exposures would be lowest and,

consequently, the contribution from dietary exposure would be the greatest. At these distances, dietary and drinking water exposures contributed more to total exposure than in handlers because the exposure from drift was comparatively lower. This was especially true for children because their dietary exposure was higher. The largest change in the combined MOEs when dietary and drinking water exposures were aggregated was in children with ground application with a low boom at 0.25 lb/A because the drift exposure was so low (combined MOEs for drift alone > 1,000).

Table 26. Aggregate Margins of Exposure for Adult and Child Bystanders [a]

Rate (lb/A)	Equipment	Adult			Child		
		Combined MOE Drift	Combined MOE Diet+Water	Combined MOE Total	Combined MOE Drift	Combined MOE Diet+Water	Combined MOE Total
Aerial Application at 1000 ft.							
0.25	**Fixed wing**	86	10,000	85	31	3,300	31
	Helicopter	95	10,000	95	35	3,300	35
0.50	**Fixed wing**	60	10,000	60	22	3,300	21
	Helicopter	68	10,000	68	25	3,300	25
Ground Application at 250 ft.							
0.25	**Fixed wing**	3,900	10,000	2,800	980	3,300	750
	Helicopter	8,600	10,000	4,700	3,500	3,300	1,700
0.50	**Fixed wing**	1,900	10,000	1,600	490	3,300	420
	Helicopter	4,300	10,000	3,000	1,800	3,300	1,100

[a] MOE = Margin of Exposure = NOEL or BMDL/Exposure. Combined MOE = $1/(1/MOE_{dermal}+1/MOE_{inhalation})$. MOEs were rounded to two significant figures. The BMDL10 of 2.1 mg/kg/day was used to evaluate dermal exposure based on brain ChE inhibition in female rats in 28-day dermal study. MOE was calculated using the absorbed dermal NOEL of 918 µg/kg/day which assumed a dermal absorption of 43.7% for the rat (Ngo, 2015). No adjustment was made for exposure period since the human exposure (1.5 hrs) was less than the animal exposure (6 hrs). The $BMDL_{10}$ for inhalation exposure is 0.42 µg/L based on brain ChE inhibition in male and female rats in 28-day inhalation study (Blair, 2010). Assuming a rat breathes 40 L/kg/hr and rats were exposed 6 hrs, the absorbed inhalation NOEL is 0.101 mg/kg/day. The $BMDL_{10}$ for acute oral exposure is 0.03 mg/kg/day based on brain ChE inhibition in PND8 rat pups (Moxon, 2003a). Bystander exposure dosages are from Tables 7-9 in the EAD for dicrotophos (Appendix V). Dietary and drinking water exposure dosages are from Table 18 in this RCD.

V. RISK APPRAISAL

V.A. Hazard Identification

HHAB considers brain ChE inhibition to be indicative of overt toxicity since it is one of the primary functional target sites and more subtle central neurological signs, such as memory and learning losses, may not be easily detected in animals unless they are specifically tested for these effects.

Worker and bystander exposures were evaluated using the dermal and inhalation NOELs from 28-day dermal and inhalation studies in rats, respectively. Because the brain ChEI was not measured until the end of the study, the NOELs used for evaluating the acute or short-term exposure by these routes are probably lower than they would have been if brain ChEI was measured after a single dose. When comparing the acute oral NOELs for brain ChEI with subchronic and chronic oral NOELs, the acute NOELs were 3 to 20 fold higher (Rattray, 1995; Brammer, 2002a; Brammer, 2002c, Horner, 1995; Allen, 1998). Based on differences seen with

oral exposure, the acute dermal and inhalation NOELs and MOEs for dicrotophos are likely to be 3-20 fold higher than estimated from the 28-day studies by these routes. On the other hand, the dermal NOEL for brain ChEI in infants and children is probably 2-7 fold lower than for adults based on a comparisons of the oral NOELs for brain ChEI in pups and adults (Moxon, 2003a vs. Rattray, 1995; Brammer, 2002a). Therefore, the acute dermal NOEL in neonates is probably fairly similar to the subchronic dermal NOEL in adult rats, which was used for evaluating child bystander exposure. Therefore, no additional uncertainty factor for infants and children was deemed necessary for evaluating acute dermal exposure for child bystanders.

V.B. Exposure Assessment

V.B.1. Dietary and Drinking Water Exposure

U.S.EPA conducted dietary assessments for dicrotophos based on its use on cotton in their recent risk assessments (U.S. EPA, 2014b, 2015c). There are only two tolerances for dicrotophos – cottonseed (0.2 ppm) and cotton gin by-products (2.0 ppm). Even though cotton gin byproducts can be fed to livestock, US EPA did not set tolerances for meat or milk. In U.S. EPA's 2014 dietary assessment, the residue levels in cottonseed oil were set to the tolerances and it was assumed that 100% of the crop was treated. In their 2015 revised dietary assessment, U.S. EPA based cottonseed oil residues on field trial studies rather than on tolerances. This was done presumably because U.S. EPA is now adding an additional uncertainty factor for all OPs due to concerns about developmental neurotoxicity, even though guideline developmental neurotoxicity studies show no increased sensitivity in young animals (U.S. EPA, 2015d). So while both the dietary and drinking water exposure values decreased in these revised estimates, the % population adjusted dose (PAD[3]) increased because of the additional FQPA UF. In their revised assessment, U.S. EPA showed that the dietary exposure estimates alone and the %PAD never exceeded 25% for any population subgroup for either acute or steady-state exposure. U.S. EPA did not cite the registrant field trial studies from which they derived their cottonseed oil residue values, but used a residue value of 0.043 ppm for both acute and steady state exposure presumably because cottonseed oil is a blended product. U.S. EPA did not cite the residue studies it used to derive this value, so DPR determined its own average cottonseed residue value of 0.040 ppm based on residues found in the undelinted cottonseed samples from drier states like California (Prochaska, 1998a). The use of undelinted cottonseed residues instead of residues in refined cottonseed oil most likely exaggerated the dietary exposure based on the residue study of cotton processed commodities. In addition, using a point value or deterministic approach for the dietary exposure also exaggerated the dietary exposure. Using an average value for acute exposure instead of the highest value in the acute dietary exposure is appropriate for refined cottonseed oil since it is a blended commodity.

U.S. EPA's drinking water exposure estimates were not shown independent of the dietary exposure. In their drinking water assessments, U.S. EPA provided model output for surface

[3] Population Adjusted Dose (PAD) is a Reference Dose (RfD) that has been divided by an additional uncertainty factor that only applies to certain populations. US EPA considers that there are risks of concern when the estimated dietary risk exceeds 100% of the PAD.

water as estimated drinking water concentrations (EDWCs) at 1-in-10 year peak, 1-in-10 year 21-day average, and 1-in-10 year annual average using the maximum and typical application rates (U.S. EPA, 2014c, 2015e). The 1-in-10 year values are equivalent to the 90th percentile estimate. In the 2015 revised assessment, the peak values ranged from 1.62 ppb for average application rate in North Carolina to 8.75 ppb for the maximum application rate in Texas. The 21-day average ranged from 1.05 ppb (typical application rate North Carolina) to 4.94 ppb (maximum application rate North Carolina). The annual values ranged from 0.0901 ppb (average application rate North Carolina) to 0.507 ppb (maximum application rate North Carolina). U.S. EPA justified its drinking water modeling based on surface water monitoring data from USGS National Water-Quality Assessment Program (NAWQA) and USDA PDP, which detected dicrotophos in 57 of 8,500 samples from seven states (Colorado, Georgia, Louisiana, Minnesota, Mississippi, North Carolina and Texas). The highest residue was 6.83 ppb in a sample from a cotton growing region of Mississippi in 2005. All other concentrations were less than 0.3 ppb. Also, USGS did not monitor the surface water in northwest Texas which is one of the largest cotton growing areas in the United States.

DPR has concerns that U.S. EPA's surface water modeling may have exaggerated the drinking water risks for several reasons. First, U.S. EPA modeled steady state surface water exposure using several different application rates including the maximum application rate. It should be noted that the %PAD did not exceed 100 for any population subgroup for acute exposure except for infants in North Carolina when the maximum application rate was used. With steady state exposure the %PAD exceeded 100 for infants and children when the maximum application rate was used in all three states and even for adult populations in North Carolina. Secondly, it seems unlikely that dicrotophos would be applied at the maximum application rate every day even for 21 days. Furthermore, the steady state exposure estimates and %PAD were reported for the 95th percentile. Again, it seems unlikely that a person would be exposed at the 95th percentile level every day for several weeks.

Because of these concerns, DPR performed its own drinking water assessment for dicrotophos by examining the PDP finished drinking water samples from 2008-2013 which were analyzed for dicrotophos. Older data were not used for the assessment because dicrotophos residues were not detected prior to 2008 and because the pre-2008 LOD was much higher (>132 ppt). DPR's MOEs for acute and steady state drinking water exposure were all greater than 1,000.

U.S. EPA did not include California EDWCs for the 2015 drinking water assessment. However, it is possible to estimate the California values by adjusting the California EDWCs in 2014 assessment by the ratio of the change in the percent cropped area from 2015 to 2014 (i.e., 21/33). So the California cotton max peak value would become 4.4 ppb. No typical application rate EDWCs were included in the 2014 assessment. However, the typical application rate EDWCs in the 2015 assessment ranged from 23 to 74% of the maximum application rate for the same state. Therefore, a California typical rate peak value is approximately 2.2 ppb (~50% of max rate peak value). The 21-day estimates in the 2015 drinking water assessment were approximately 52-65% of the peak values. Since DPR generally uses average values for seasonal exposure rather than an upper end estimate, then the 21-day average EDWC at the typical application rate is estimated to be 1.1 ppb (~50% of peak value at typical application rate). These estimates were used to perform a deterministic drinking water assessment for dicrotophos. The resultant acute

drinking water MOEs ranged from 37 for infants to 98 for children 3-5 years old. The other population subgroups had MOEs greater than 100, but less than 200. The steady state MOEs were larger, with most adult population subgroups having MOEs greater than 1,000. However, the steady state MOEs for infants and children were still less than 1,000, ranging from 346 (infants) to 888 (children 3-5 years old). Using a deterministic approach for the drinking water analysis with these California estimates resulted in much higher exposure estimates than if a probabilistic approach had been used. Since U.S. EPA did not include its residue distribution files in their 2014 or 2015 assessments, it is not possible to perform a probabilistic analysis on the data.

There are uncertainties when using both sources of drinking water data. Because USGS has a set sampling schedule, these samples may miss peak concentrations, especially if the sampling schedule does not capture high agricultural use. In addition, solely relying on U.S. EPA drinking water modeling data is problematic because it is unknown to what level the model has been validated against empirical data. Both the USGS surface water monitoring and the U.S. EPA surface water model may overestimate drinking water exposure because they represent water concentrations that are upstream of water treatment plants where dicrotophos is likely to be further diluted and degraded during treatment before being delivered as tap water.

V.B.2. Occupational and Bystander Exposure

The uncertainties associated with the occupational and bystander exposure estimates are discussed in the Exposure Appraisal section of the EAD (Appendix V).

V.C. Risk Characterization

Generally, an MOE of at least 100 is considered by HHAB to be sufficiently protective of human health when the NOEL for an adverse effect is derived from an animal study. Built into the MOE cutoff of 100 is the assumption that humans are 10 times more sensitive than animals and that there is a 10-fold variation in sensitivity between the lower range of the normal distribution in the overall population and the sensitive subgroup (Dourson *et al.*, 2002). All of the NOELs for dicrotophos are derived from animal studies.

The dietary and drinking water MOEs for all population subgroups were greater than 1,000 when considered separately or combined with either acute or steady state exposure.

Among the handler scenarios, the dermal MOEs were all less than the target MOE of 100, except for seasonal exposure for ground boom mixer/loaders and applicators and scouts. The inhalation MOEs for handlers were always higher than their corresponding dermal MOEs and often greater than the target MOE of 100. A few scenarios for aerial application had inhalation MOEs less than 100 including short-term and seasonal exposure for mixer/loaders and short-term exposure for flaggers.

For the adult bystanders, the dermal MOEs from spray drift were above the target MOE of 100 at 25 ft. or more from the field edge for all ground boom application scenarios and for aerial application when applied at 0.25 lb AI/acre. When applied at 0.5 lb AI/acre, the dermal MOEs

were greater than 100 at 50 ft or greater from the application site. The inhalation MOEs for adult bystanders with aerial application were less than 100 except with aerial application at 0.25 lb AI/acre with a helicopter at 1,000 ft from the field edge. It is uncertain if the inhalation MOEs with ground boom application would be above the target MOE since the inhalation exposure for this application method could not be calculated.

For child bystanders exposed to dicrotophos cotton spray drift, the oral MOEs were greater than 100 at 25 ft. from the field edge, except for all hand-to-mouth exposures with aerial application and ground boom application when applied at 0.5 lb AI/acre with a high boom. With aerial application the oral MOEs were greater than 100 at 250 ft and 500 ft from the field edge when applied at 0.25 and 0.5 lb AI/acre, respectively. The oral MOEs were greater than 100 at 50 ft with ground boom application when applied at 0.5 lb AI/acre with a high boom. The dermal MOEs for child bystanders were also greater than 100 at 25 and 100 ft from field edge when applied aerial at 0.25 and 0.5 lb AI/acre, respectively. With ground boom application, the dermal MOEs were all greater than 100 at 25 ft from the field edge. The inhalation MOEs for child bystanders were significantly less than the target of 100 for all aerial application scenarios up to 1,000 ft. from the field edge which resulted in the combined MOEs all being less than 100. Since inhalation exposure could not be estimated for ground boom application, it is uncertain if the MOEs for this route of exposure were above or below the target of 100.

V.D. U.S. EPA Human Health Risk Assessment for Dicrotophos

In 2014, U.S. EPA completed a human health risk assessment for dicrotophos use on cotton; this was later revised in 2015 (U.S. EPA, 2014a, 2015a). In conducting DPR's risk assessment, the endpoints and BMD analysis were examined to see if HHAB concurred with U.S. EPA's selection of critical NOELs for calculating their MOEs. There were no changes in U.S. EPA's critical NOELS between the 2014 and 2015 assessments. DPR had received most of the studies that U.S. EPA cited in its risk assessment. HHAB agreed with U.S. EPA regarding the benchmark response selected for the BMD analysis; that is, a 10% relative deviation in the brain ChEI using the continuous models. However, HHAB differed from U.S. EPA with regards to which models were included in the BMD analysis. U.S. EPA limited its approach to four exponential models based on the National Academy of Science's recommendation for the cumulative risk assessment for the organophosphate pesticides (U.S. EPA, 2002). HHAB decided to include the Michaelis-Menten or Hill model in addition to the exponential models because it is consistent with a receptor-mediated response. In a number of cases, the Hill model fit the data better than any of the exponential models. For this reason, HHAB obtained a lower $BMDL_{10}$ value (0.03 mg/kg/day vs 0.07 mg/kg/day) for brain ChEI in the comparative ChE study in 8-day old male pups based on the Hill model. This $BMDL_{10}$ was used as the critical NOEL to evaluate the short-term oral exposure to dicrotophos from spray drift in children. The critical NOELs selected by the two agencies for this risk assessment for dicrotophos are summarized in Table 27.

Other more significant differences in the critical NOELs used by U.S. EPA and HHAB were the result of differences in the assumptions about the dermal absorption and exposure duration. U.S. EPA and HHAB started with the same $BMDL_{10}$ of 2.1 mg/g/day from the 28-day dermal toxicity study for dicrotophos as the dermal NOEL, but U.S. EPA adjusted this dermal NOEL upwards

based on the difference in *in vitro* dermal penetration between humans and rats, resulting in a 4.4 times higher dermal NOEL. HHAB reviewed the same studies, but derived different absorption rates in rats and humans because in the calculation of the dermal absorption DPR included the residues in the epidermis and stratum corneum in the percent absorbed both *in vitro* (added to the residues in the acceptor fluid) and *in vivo* (added to the residues in urine, feces, cage wash, carbon dioxide and charcoal traps, GI contents and carcass), whereas U.S EPA did not. Therefore, HHAB estimated the mean *in vitro* dermal absorption in rats and humans to be 53.9 and 19.0 % compared to U.S. EPA estimates of 47.1 and 10.6%, respectively. HHAB estimated the *in vivo* dermal absorption in rats to be 43.7% compared to U.S. EPA's estimate of 32.9%. In addition, HHAB differed from U.S. EPA by calculating an upper end estimate for human *in vivo* dermal absorption rather than use the ratio of the mean values for *in vitro* dermal absorption in rats to humans. An upper end estimate was calculated because the human *in vivo* dermal absorption was not actually measured unlike with rat *in vivo* dermal absorption. Therefore, HHAB used a human dermal absorption value of 26.3% for estimating exposure. Consequently, the ratio of the *in vivo* rat to human dermal absorption used by HHAB was 1.7 compared to U.S. EPA's ratio of 4.4 for the ratio of *in vitro* rat to human dermal absorption. U.S. EPA's dermal MOEs could be 2.5 times higher than HHAB's just from different assumptions about the dermal absorption in rats and humans. Besides adjusting for rat *in vivo* dermal absorption, HHAB also adjusted the dermal NOEL for differences in exposure duration between rats and humans (6 hrs vs. 8 hrs). U.S. EPA did not make any adjustments for exposure duration between animals and humans. The combined differences in assumptions about the dermal absorption and exposure duration accounted for approximately a 3.5-fold difference in the dermal MOEs used by the two agencies. However, the differences in the seasonal/steady-state dermal MOEs calculated by the two agencies were much larger, especially for applicators and flaggers with aerial application. For these scenarios, U.S. EPA's MOE was 24 fold higher for applicators and 39 fold higher for flaggers, indicating there were additional differences in how the dermal exposure estimates were calculated (Table 28). The differences in the exposure estimates between these two agencies are discussed in the exposure appraisal section of the EAD (Appendix V).

The $BMDL_{10}$ values derived for brain ChEI in the 28-day inhalation study for this risk assessment differed from U.S. EPA's $BMDL_{10}$ (M - 0.62 µg/L, F – no fit) even with the exponential models because it appears U.S. EPA incorrectly entered 10 animals/sex/dose in their BMD analysis even though only 5 animals/sex/dose were analyzed for ChE activity. HHAB also differed from U.S. EPA in the conversion of the air concentration to mg/kg/day, in that U.S. EPA assumed an hourly breathing rate of 43.5 L/kg/hr to obtain an absorbed dose of 0.162 mg/kg/day (0.62 µg/L x 6 hr/day x 43.5 L/kg/hr). HHAB used a breathing rate of 40 L:/kg/day, resulting in an absorbed dose of 0.101 mg/kg/day (0.42 µg/L x 6 hr/day x 40 L/K/hr). These differences in assumptions about breathing rate and exposure duration accounted for a 1.5 fold difference in MOEs. U.S. EPA's inhalation MOEs were approximately 10-fold higher for aerial applicators and flaggers. U.S. EPA did not calculate short-term MOEs for workers.

Table 27. Comparison of DPR RAS and U.S. EPA HED Critical Endpoints, NOELs/BMDLs and Adjustments Factors for Dicrotophos

Exposure Duration	Critical Endpoints	NOEL/BMDL (mg/kg/day)		Adjustments	
		DPR RAS	U.S. EPA HED	DPR RAS	U.S. EPA HED
Dermal Route - Adults					
Short-term	Brain ChEI in female rats after 28-day dermal exposure	2.1	NA	Rat dermal absorption ↓ 43.7% Exposure duration differences- ↓ 25%	NA
Seasonal	Brain ChEI in rats after 28-day dermal exposure	2.1	2.1	Rat dermal absorption ↓ 43.7% Exposure duration differences- ↓ 25%	Relative human dermal absorption – ↑ 4.4 X
Inhalation Route - Adults					
Short-term	Brain ChEI in male and female rats after 28-day inhalation exposure	0.42 µg/L	NA	100% absorption, 40 L/kg-hr rat breathing rate	NA
Seasonal	Brain ChEI in male and female rats after 28-day inhalation exposure	0.42 µg/L	0.62 µg/L	100% absorption, 40 L/kg-hr rat breathing rate	100% absorption, 43.5 L/kg-hr rat breathing rate
Oral and Dermal Route - Children					
Short-term	Brain ChEI in rat pups (PND 12-18 exposure)	0.03	0.07	None	None
Carcinogenicity					
Long-term	Follicular cell thyroid tumor in male mice	Insufficient evidence	Insufficient evidence		

Table 28. Comparison of Margins of Exposure Calculated by DPR RAS and U.S. EPA HED for Handlers Involved in Application of Dicrotophos to Cotton

	Dermal MOE [a]				Inhalation MOE			
	Short-term		Long-term/Steady-state		Short-term		Long-term/Steady-state	
	DPR RAS [b]	U.S. EPA [c]	DPR RAS [b]	U.S. EPA [c]	DPR RAS [d]	U.S. EPA [e]	DPR RAS [d]	U.S. EPA [e]
Aerial Application								
Mixer/Loaders	6	NC	17	120	27	NC	75	220
Applicators	8	NC	21	520	130	NC	360	3,800
Flaggers	3	NC	9	350	59	NC	170	1,800
Ground boom Application								
Mixer/Loaders	36	NC	100	750	160	NC	450	1,400
Applicators	88	NC	250	1,300	490	NC	1,400	2,600
Scouts	72	NC	1,200	4,600	NC	NC	NC	NC

[a] MOE = Margin of Exposure = NOEL or BMDL/Exposure. Rounded to two significant figures. Exposure dosages are from Tables 4-6 in the EAD document for dicrotophos (Appendix V).
[b] $BMDL_{10}$ = 2.1 mg/kg/day based on brain ChE inhibition in female rats in 28-day dermal study (Noakes, 2001). Assuming a rat dermal absorption of 43.7% and adjusting for 6 hr exposure in rats versus 8-hr exposure in workers, the absorbed dermal NOEL = 0.69 mg/kg/day.
[c] $BMDL_{10}$ = 2.1 mg/kg/day based on brain ChE inhibition in female rats in 28-day dermal study (Noakes, 2001). After adjusting for interspecies differences in dermal absorption (rats absorb 4.4 X more than humans) based on triple pack study, the external dermal NOEL = 9.3 mg/kg/day. There was no adjustment for differences in exposure duration between animals and humans.
[d] $BMDL_{10}$ = 0.42 µg/L based on brain ChE inhibition in male and female rats in 28-day inhalation study (Blair, 2010). Assuming a rat breathes 40 L/kg/hr and rats were exposed 6 hrs, the inhalation NOEL is 0.101 mg/kg/day.
[e] $BMDL_{10}$ = 0.67 µg/L based on brain ChE inhibition in male and female rats in 28-day inhalation study (Blair, 2010). Assuming rats were exposed 6 hrs and breathes 43.5 L/kg/hr, the inhalation NOEL is 0.175 mg/kg/day.
NC = Not calculated

V.E. Issues Related to the Food Quality Protection Act

V.E.1. Pre- and Post-natal Sensitivity

In this risk assessment, children being potentially at higher risks for adverse effects from dicrotophos exposure when compared to adults was accounted for in part by using age-specific parameters such as breathing rates in the exposure calculation. For example, infants when compared to adults have higher inhalation exposure because of their higher breathing rates. Some reproductive effects were seen at high doses in rats in the 28-day inhalation study and in the reproductive toxicity study (Blair, 2010). Seminiferous tubules atrophy in the testes was seen in 2 of 10 males at the high dose, 2.9 µg/L, compared to none in the controls (Blair, 2010). However, brain ChEI was a more sensitive endpoint in this study, with a LOEL of 0.73 µg/L. In the reproductive toxicity study, reduced fertility indices were seen in the F_0 dams at the high doses (15 and 25 ppm) (Moxon, 1997). Pup viability indices were also reduced in this study in a dose-related manner at 5 ppm and higher. The effects on the fertility indices and pup viability indices could be due to indirect effects of the neurotoxicity rather than direct effects on the reproductive organs since no histological changes were observed in the reproductive organs in this study (Moxon, 1997). ChE activity was not measured in this study. Regardless, the reproductive and pup LOELs in this study were equal to or higher than the parental LOEL which was based on reduced body weight. Therefore, no additional uncertainty factor is needed to protect against these reproductive effects.

Dicrotophos was not teratogenic in rats or rabbits (Rodwell, 1986; Moxon, 2001). In these developmental toxicity studies, the fetal NOELs were higher than the maternal NOELs. The only fetal effect observed was reduced body weights at the high dose in rabbits. In a developmental neurotoxicity study in rats, the NOELs for dams and pups were the same since no neurobehavioral effects were seen at the high dose (Brammer, 2003). ChE activity was not measured in any of the developmental studies, including the main developmental neurotoxicity study. However, in a preliminary developmental neurotoxicity study where ChE activities were measured in the brain and RBC of dams and fetuses (GD22), the maternal LOEL for ChEI was lower (0.05 mg/kg/day) than for fetuses (0.2 mg/kg/day) (Brammer, 2003).

The comparative ChE studies in weanling and young adult rats did show some slightly greater sensitivity to ChEI around 2-7 fold. But since the lowest NOEL for ChEI in PND8 pups (Moxon, 2003a) was used for the acute NOEL to evaluate child bystander oral exposure, no additional FQPA factor is considered necessary to protect against increased sensitivity in infants and children. U.S. EPA came to the same conclusion after examining the same developmental and reproductive toxicity data (U.S. EPA, 2014a). A NOEL for ChEI in adult rats was used to evaluate acute dermal exposure in child bystanders, but this dermal NOEL was from a 28-day dermal toxicity study (Noakes, 2001). Comparison of the acute oral and subchronic/chronic oral NOELs indicate the acute NOELs were 3 to 20 fold higher (Rattray, 1995; Brammer, 2002a vs. Brammer, 2002c, Horner, 1995; Allen, 1998). On the other hand, a comparison of the oral NOELs for brain ChEI in pups and adults suggested the acute NOEL for ChEI in infants and children is probably 2 to7 fold lower than for adults (Moxon, 2003a vs. Rattray, 1995; Brammer, 2002a). Therefore, the acute dermal NOEL in pups is similar to the subchronic dermal NOEL in

adult rats, so no additional uncertainty factor for infants and children was deemed necessary for evaluating acute dermal exposure for child bystanders.

In September 2015, U.S. EPA released a systematic review of the literature for effects of organophosphate (OP) pesticides on neurodevelopment (U.S. EPA, 2015d). Much of this literature review was initiated as part of the U.S. EPA's chlorpyrifos risk assessment. This systematic review elucidated other potential modes of action (MOAs) or adverse outcome pathways (AOPs) than AChEI for organophosphate pesticides to affect neurodevelopment. Multiple plausible MOAs were being evaluated by researchers including AChE as a morphogen, cholinergic system, endocannabinoid system, reactive oxygen species, serotonergic system, tubulin, microtubule associated proteins, and axonal transport. No one pathway had sufficient data to be considered more plausible than the others. Some of the neurodevelopmental effects studied appear to be as or more sensitive than AChEI. Many of the *in vivo* animal studies and epidemiology studies reviewed included exposure to and potential neurodevelopmental effects from OPs besides chlorpyrifos, including parathion, diazinon, methyl parathion, methamidophos, chlormephos, dichlorvos, fenitrothion, and oxydemeton-methyl. Three major epidemiology studies were reviewed including one from the Columbia University Center for Children's Environmental Health (CCCEH), study, the Mount-Sinai Center for Children's Environmental Health, and the University of California, Berkeley CHAMACOS (Center for the Health Assessment of Mothers and Children of Salinas) study. As a result of this systematic review, U.S. EPA developed a new policy for individual OP risk assessments which requires that an additional 10X be applied to all scenarios except for dietary exposure for adults 50-99 years old to protect against possible neurodevelopmental effects due the uncertainty about the MOA/AOP. U.S. EPA applied this new policy to their revised risk assessment for dicrotophos (U.S. EPA, 2015a). HHAB supports U.S. EPA's use of an additional uncertainty factor of 10 for OPs based on their systematic review of potential neurodevelopmental effects and their mechanisms.

V.E.2. Cumulative Toxicity

The cumulative toxicity of dicrotophos with other organophosphate pesticides has been addressed by U.S. EPA in their cumulative risk assessment for OPs (U.S. EPA, 2006b). No additional analysis was performed by HHAB.

V.E.3. Endocrine Disruption Effect

The Food Quality Protection Act (FQPA) of 1996 required U.S. EPA to develop a screening program to determine the endocrine disruption potential of pesticides. In 1997, the U.S. EPA Risk Assessment Forum published a report that reviewed the current state of science relative to environmental endocrine disruption (U.S. EPA, 1997). U.S. EPA formed the Endocrine Disruptor Screening and Testing Advisory Committee (EDSTAC) to develop a strategy for screening and testing of pesticides for their potential to produce endocrine disruption. The EDSTAC members include various stakeholders and scientific experts. This screening and testing process was implemented in August 1999 as required by FQPA. The interim science policy stated in U.S. EPA's 1997 report is that "*the Agency does not consider endocrine disruption to be an adverse endpoint per se, but rather to be a mode or mechanism of action leading to other outcomes*."

Dicrotophos exposure resulted in an increase in follicular cell thyroid tumors in male mice. This could be an indication of endocrine disruption. However, the ToxCast assays for the thyroid receptor were negative. Several ToxCast assays were positive indicating some disruption in inflammatory signaling and inhibition of at least one CYP enzyme which could lead to an increased incidence of follicular cell thyroid tumors by interfering with the metabolism of the thyroid hormone (Kleinstreuer *et al.*, 2013). There was one positive assay for the estrogen receptor, but this is of questionable significance since it was the only positive result. Other possible estrogenic and/or androgenic effects were seen in several *in vivo* animal studies, including seminiferous tubules atrophy in the testes of male rats at the high dose in the 28-day inhalation study (Blair, 2010). In the reproductive toxicity study, a reduced fertility index was seen at the high dose (Moxon, 1997). Pup viability was also reduced in a dose-related manner in this study. The only fetal effect seen in the developmental toxicity studies was reduced fetal body weights at the high dose in rabbits (Moxon, 2001). Since these effects all occurred at high doses above those that elicited significant ChEI, they could be secondary effects related to ChEI rather than the result of endocrine disruption.

VI. CONCLUSIONS

The potential for dicrotophos use on cotton to result in adverse health effects in humans was evaluated in this risk assessment.

The dietary and drinking water MOEs for all population subgroups were all greater than 1,000 when considered separately or combined with either acute or steady state exposure.

The dermal MOEs for handlers were less than the target of 1000 for female workers of childbearing age for all scenarios. The handlers MOEs were even less than 100 for all scenarios except for scouts, so this exposure is a concern even for adult males.

The inhalation MOEs for handlers was greater than 100 for most scenarios except aerial mixer/loaders (short-term and steady-state) and flaggers (short-term only). However, the inhalation MOEs were less than 1,000 for all scenarios except seasonal exposure for ground boom applicators so they are a concern for female workers of reproductive age. The combined dermal and inhalation MOEs were similar to the dermal MOEs since dermal exposure was much greater (Conclusion Table 1).

The dermal MOEs for adult bystanders were all greater than 100 at 25 ft with ground boom application and with aerial application when applied at 0.25 lb AI/acre. The dermal MOEs were greater than 1,000 at 250 ft for all ground boom scenarios and at 1,000 ft. with aerial application at 0.25 lb AI/acre. With aerial application, the inhalation MOEs for all adult bystander scenarios were less than 100 even at 1,000 ft., except when applied by helicopter at 0.25 lb AI/acre. None of the inhalation MOEs were greater than 1,000 at 1,000 ft.

The dermal, inhalation and oral MOEs for child bystanders were all greater than 1,000 with ground boom application using a low boom at 100 ft. from the field edge. With high boom equipment, child bystanders did not have MOEs greater than 1,000 at even 250 ft. from the field

edge when applied at 0.5 lb AI/acre. With aerial application, child bystanders inhalation MOEs were below 100 even at 1,000 ft. from the field edge. Dermal MOEs for most child bystander scenarios were also less than 1,000 even at 1,000 ft. Oral MOEs tended to be higher, but some activities like hand-to-mouth activity had MOEs that were still less than 1,000 at 1,000 ft from the field edge (Conclusion Table 2).

Risk Appraisal

Dietary exposure represented the "high-end" of the potential exposure because it was based on a deterministic approach using average residues from residue studies on unprocessed undelinted whole cottonseed and it assumed that 100% of the crop was treated. The use of pesticide residue data from the US Department of Agriculture (USDA) Pesticide Data Program (PDP) on finished drinking water may lead to an underestimation of the exposure, because PDP may not detect peak pesticide concentrations in drinking water. The DPR surface and ground water programs currently do not monitor dicrotophos since is not registered for use in California.

The MOEs for acute dermal and inhalation exposure in workers and adult bystanders were based on NOELs/BMDLs for subchronic dermal and inhalation studies. Comparison of the oral acute and subchronic NOELs/BMDLs indicate the acute NOELs/BMDLs were 3 to 20 fold higher than the subchronic NOELs/BMDLs. Based on these differences with oral NOELs/BMDLs, the acute dermal and inhalation NOELs/BMDLs and MOEs for dicrotophos are likely to be 3 to 20 fold higher than estimated from the 28-day studies by these routes. On the other hand, the dermal NOEL/BMDL is probably 2 to 7 fold lower in infants and children than for adults based on comparisons of the oral NOELs/BMDLs for brain ChEI in pups and adults.

Therefore, the acute dermal NOEL/BMDL in neonates is probably close to the subchronic dermal NOEL/BMDL in adult rats, which was used for evaluating child bystander exposure.

U.S. EPA and HHAB calculations would occasionally generate different results for the BMD analysis of the brain ChE data because U.S. EPA only used the exponential model and HHAB included the Hill model, which often provided a better fit. Both agencies selected the same study and endpoint to evaluate acute oral exposure in children, but HHAB derived a BMDL of 0.03 mg/kg/day using the Hill model, which is 2-fold lower than the BMDL of 0.07 mg/kg/day derived by U.S. EPA with the exponential model.

U.S. EPA and HHAB obtained the same BMDL for the 28-day dermal study using the exponential model, but U.S. EPA multiplied the BMDL by the ratio of the *in vitro* dermal absorption rate in rats to humans (4.44) to obtain a "Refined Dermal Equivalent Dose (RDD)" for humans. Using the same studies, HHAB estimated different dermal absorption rates for rats and humans by including the residues in the epidermis and stratum corneum in the "absorbed dose." In addition, HHAB used an upper end estimate of the in vivo human dermal absorption to adjust the exposure dosages because in vivo human dermal absorption was not actually measured. The ratio of the *in vivo* dermal absorption in rats to humans used by DPR was approximately 1.7. This difference in dermal absorption assumptions resulted in U.S. EPA's dermal MOEs being approximately 3-fold higher than those of DPR.

U.S. EPA and HHAB obtained different BMDLs for the 28-day inhalation study using the same exponential model because U.S. EPA assumed 10 animals/sex/dose when only 5 animals/sex/dose had ChE activity measured. In addition, different breathing rate assumptions were made when converting the BMDL expressed as air concentration to mg/kg/day (U.S. EPA - 43.5 L/kg/hr; HHAB - 40 L:/kg/day). These differences resulted in U.S. EPA's inhalation NOEL being 75% higher than DPR's inhalation NOEL.

In addition to differences in assumptions about dermal absorption, DPR's handler MOEs for dicrotophos were significantly different from U.S. EPA's because: 1) HHAB used upper confidence limits on both the 95th and mean exposure estimates whereas U.S. EPA used the mean; 2) U.S. EPA used the Agricultural Handler Exposure Task Force (AHETF) database while HHAB used the Pesticide Handler Exposure Database (PHED) to estimate handlers exposure.

Conclusion Table 1. Aggregate Margins of Exposure for Handlers

Scenario	Acute			Seasonal		
	Combined MOE [a] Occupation	Combined MOE Diet+Water	Combined MOE Total	Combined MOE Occupation	Combined MOE Diet+Water	Combined MOE Total
Aerial Appplication						
Mixer/loaders	5	10,000	5	14	28,000	14
Applicators	8	10,000	8	21	28,000	20
Flaggers	3	10,300	3	9	28,000	9
Ground Application						
Mixer/loaders	29	10,000	29	82	28,000	82
Applicators	75	10,000	74	210	28,000	210
Post-application						
Scouts	140	10,000	130	2,300	28,000	2,100

[a] MOE: Margin of Exposure = [NOEL or BMDL]/Exposure. Combined MOE = $1/(1/MOE_{dermal}+1/MOE_{inhalation})$. The $BMDL_{10}$ for dermal exposure was 2.1 mg/kg/day. The absorbed dermal NOEL was 0.69 mg/kg/day. The $BMDL_{10}$ for inhalation exposure was 0.42 µg/L . The absorbed inhalation NOEL is 0.101 mg/kg/day. The $BMDL_{10}$ for oral acute exposure is $BMDL_{10}$ is 0.03 mg/kg/day. The $BMDL_{10}$ for seasonal/steady-state exposure is 0.025 mg/kg/. For more details see Table 25. Occupational exposure dosages are from Tables 4-6 in the EAD for dicrotophos (Appendix V). Dietary and drinking water exposure dosages are from Table 20 in this RCD.

Target MOE = 1000

Conclusion Table 2. Aggregate Margins of Exposure for Adult and Child Bystanders

Rate (lb/A)	Equipment	Adult			Child		
		Combined MOE [a] Drift	Combined MOE Diet+Water	Combined MOE Total	Combined MOE Drift	Combined MOE Diet+Water	Combined MOE Total
Aerial Application at 1000 ft.							
0.25	**Fixed wing**	86	10,000	85	31	3,300	31
	Helicopter	95	10,000	95	35	3,300	35
0.50	**Fixed wing**	60	10,000	60	22	3,300	21
	Helicopter	68	10,000	68	25	3,300	25
Ground Application at 250 ft.							
0.25	**Fixed wing**	3,900	10,000	2,800	980	3,300	750
	Helicopter	8,600	10,000	4,700	3,500	3,300	1,700
0.50	**Fixed wing**	1,900	10,000	1,600	490	3,300	420
	Helicopter	4,300	10,000	3,000	1,800	3,300	1,100

[a] MOE = Margin of Exposure = NOEL or BMDL/Exposure. Combined MOE = $1/(1/MOE_{dermal}+1/MOE_{inhalation})$. The BMDL10 of 2.1 mg/kg/day was used to evaluate dermal exposure. MOE was calculated using the absorbed dermal NOEL of 918 µg/kg/day. The $BMDL_{10}$ for inhalation exposure is 0.42 µg/. The absorbed inhalation NOEL is 0.101 mg/kg/day. The $BMDL_{10}$ for acute oral exposure is 0.03 mg/kg/day. For more details see Table 26. Bystander exposure dosages are from Tables 7-9 in the EAD (Appendix V). Dietary and drinking water exposure dosages are from Table 18 in this RCD.

Target MOE=1000

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Appendix I. DPR's SB950 Summary of Toxicology Data for Dicrotophos

CALIFORNIA ENVIRONMENTAL PROTECTION AGENCY
DEPARTMENT OF PESTICIDE REGULATION
MEDICAL TOXICOLOGY BRANCH

SUMMARY OF TOXICOLOGY DATA
DICROTOPHOS

Chemical Code # 72, Document Processing Number (DPN) # 299
SB 950 # 60
2/6/14, revised, 3/7/14, 9/3/14, 10/8/14, and Dec. 5, 2014

DATA GAP STATUS

Chronic toxicity, rat:	No data gap, possible adverse effect
Chronic toxicity, dog:	No data gap, possible adverse effect
Oncogenicity, rat:	No data gap, no adverse effect
Oncogenicity, mouse:	No data gap, possible adverse effect
Reproduction, rat:	No data gap, possible adverse effect
Developmental toxicity, rat:	No data gap, no adverse effect
Developmental toxicity, rabbit:	No data gap, no adverse effect
Reverse mutation assay:	No data gap, no adverse effect
In vitro mammalian cell assay:	No data gap, possible adverse effect
In vivo cytogenetics assay:	No data gap, no adverse effect
Neurotoxicity:	No data gap, possible adverse effect †

† Hen neurotoxicity study did not indicate distal delayed neuropathies, but acetylcholinesterase inhibition was flagged as "possible adverse effect" in several rat studies.

Toxicology one-liners are attached.

All record numbers for the above study types through 280963 (Document No. 299-0069) were examined. This includes all relevant studies indexed by DPR as of Dec. 2, 2014.

In the 1-liners below:
** indicates an acceptable study.
Bold face indicates a possible adverse effect.
indicates a study on file but not yet reviewed.

File name: t20141205
Revised by T. Moore, 3/7/14, 9/3/14, and 10/8/14; by C. Aldous, Dec. 5, 2014

NOTE: The following symbols may be used in the Table of Contents which follows:
** = data adequately address FIFRA requirement
† = study(ies) flagged as "possible adverse effect"
N/A = study type not currently required

This record contains summaries of studies. Individual worksheets may be useful for detailed assessment.

Table of Contents

METABOLISM AND PHARMACOKINETICS ** 3
GUIDELINE ACUTE STUDIES ON ACTIVE INGREDIENT 4
Acute oral toxicity, rat ** † (flagged because Toxicity Category I) 4
Acute dermal toxicity ** 4
Acute inhalation toxicity, rat ** 4
Primary eye irritation, rabbit ** 5
Primary dermal irritation ** 5
Dermal sensitization ** 5
SUBCHRONIC STUDIES 6
Oral toxicity, rat: (No standard rat subchronic, but see 90-day neurotoxicity, below) 6
Oral toxicity, non-rodent: 6
Dermal toxicity, 21/28-day or 90-day: ** † (flagged for brain AChE inhibition) 6
Inhalation toxicity, 28-day to 90-day: (N/A) † (flagged for brain AChE inhibition) 6
CHRONIC STUDIES 7
Combined Chronic and Oncogenicity, rat ** † (flagged for brain AChE inhibition) 7
Chronic, dog ** † (flagged for reduced brain AChE activity) 8
Oncogenicity, rat (see Combined, above) 9
Oncogenicity, mouse ** † (flagged for thyroid adenomas) 9
GENOTOXICITY 10
Bacterial Reverse Mutation Assay ** 10
In Vitro Mammalian Cell Assay ** † (positive mouse lymphoma assay) 10
In Vivo Cytogenetics Assay ** 10
Miscellaneous Genotoxicity Assays (not classifiable with current guidelines) 11
REPRODUCTIVE TOXICITY, RAT ** † (flagged for excessive pup mortality) 12

DEVELOPMENTAL TOXICITY 13
Rat ** 13
Rabbit ** 13
NEUROTOXICITY 14
Acute neurotoxicity, rat ** † (flagged for brain AChE) 14
90-day neurotoxicity, rat ** † (flagged for AChE inhibition) 15
Developmental neurotoxicity, rat ** 15
Delayed neurotoxicity, hen ** 16
IMMUNOTOXICITY ** 18
ENDOCRINE DISRUPTOR STUDIES 18
MECHANISTIC STUDIES (largely acetylcholinesterase inhibition) 18

METABOLISM AND PHARMACOKINETICS **

299-0053; 276578; "Dicrotophos: Rat Metabolism Study"; (D. Wu, Z. Gu; XenoBiotic Laboratories, Inc., Plainsboro, NJ; XLB Study No. XBL94040; 2/8/96); Five or seven Crl:CD(SD)/sex/group were assigned to one of 4 groups (designated A to D) and were treated with [3-^{14}C] Dicrotophos (lot no. 836A-893, radiopurity: 98.9%, specific activity: 25.1 mCi/mmole). Non-labeled dicrotophos technical (lot no. DPAQ281, 96.0% E (cis) isomer, 1.45% Z (trans) isomer) was used to adjust the specific activity of the dosing preparations or as the dosing preparation in the multiple dose regimen. In Groups A, B and C, the rats were dosed orally by gavage. In Group D, they were injected intravenously with the test material. The Group A animals received a single dose of 0.5 mg/kg. The animals in Group B received 14 daily doses of 0.5 mg/kg of unlabeled dicrotophos and on the 15th day, a single dose of 0.5 mg/kg of the radiolabeled test material. In Group C, the animals received a single dose of 3.0 mg/kg. The Group D animals were dosed once with 0.5 mg/kg. The primary route of excretion was via the urine with the percentage of administered dose recovered from the urine ranging from 86 to 89 (urine and cage rinse) by the conclusion of the 4-day collection period irrespective of the dosing regimen. Recovery in the feces ranged from 1.5 to 5% of the administered dose. Ninety one to 95% of the administered dose was excreted within the 1st 24 hours. These data indicated that approximately 94 to 97% of the administered dose was absorbed. Analysis of the tissues at 4 days post dose or post-final dose revealed the primary site of radiolabel recovery to be the liver. In the metabolite analysis, the parent compound constituted 3 to 7% of the administered dose. The formation of monocrotophos by demethylation of one of the amide methyl groups was <1 to 3% of the dose. Cleavage of the phosphate group with the resultant formation of the acetoacetamide moiety and subsequent hydroxylation of the methyl groups and/or reduction of one of the carbonyl oxygens was the primary pathway of metabolism. **Study Acceptable**. (Moore, 8/28/14)

GUIDELINE ACUTE STUDIES ON ACTIVE INGREDIENT

Acute oral toxicity, rat ** † (flagged because Toxicity Category I)

299-0018; 45362; "Toxicology of Insecticides: The Acute Oral and Percutaneous Toxicity, Skin and Eye Irritancy and Skin Sensitizing Potential of Bidrin"; (J.B. Price; Shell Research Limited, Sittingbourne Research Centre, Sittingbourne, Kent, ME9, 8AG, England; Doc. No. SBGR.85.266; 12/12/85); Five Fischer 344 rats/sex/group were dosed orally by gavage with 5, 8, 12, 20 or 30 mg/kg of Bidrin (Dicrotophos technical) (batch no. 17-1-0-0; Dicrotophos-E content: 88.3%) (vehicle: water). The following mortality resulted from the treatment: 5 (M/F: 0/5), 8 (M: 0/5, F: 2/5), 12 (M: 4/5, F: 5/5), 20 (M/F: 5/5), 30 (M/F: 5/5). Deaths occurred within 90 minutes of dosing. Clinical signs included lacrimation, salivation, fasciculation, chromodacryorrhea, unkempt appearance, and abnormal posture. In the necropsy examination, those animals which died prematurely had discolored liquid in the stomachs and minor hemorrhages in the cranial cavity or brain surface. **Rat Oral LD50:** (M) 11 mg/kg; (F) 8 mg/kg; Toxicity Category I; **Study acceptable.** (Kahn, 3/21/86, updated Moore, 1/24/14)

Acute dermal toxicity **

299-0018; 45363; "Toxicology of Insecticides: The Acute Oral and Percutaneous Toxicity, Skin and Eye Irritancy and Skin Sensitizing Potential of Bidrin"; (J.B. Price; Shell Research Limited, Sittingbourne Research Centre, Sittingbourne, Kent, ME9, 8AG, England; Doc. No. SBGR.85.266; 12/12/85); The skin of five Fischer 344 rats/sex/group (except where noted) was exposed to 80, 125, 200, 315 (10 animals/sex), 500 (10 animals/sex), 800 or 1270 mg/kg of Bidrin (Dicrotophos technical) (batch no. 17-1-0-0; Dicrotophos-E content: 88.3%) for 24 hours under an occlusive wrap. Water was used to dilute all of the treatment preparations except for the 1270 mg/kg treatment which was undiluted. The following mortality resulted from the treatment: 80 (M/F: 0/5), 125 (M/F: 0/5), 200 (M/F: 0/5), 315 (M: 0/9 (one animal escaped during the observation period), F: 3/10), 500 (M: 0/10, F: 3/10), 800 (M: 1/5, F: 5/5), 1270 (M/F: 5/5). Clinical signs included fasciculations, chromodacryorrhea, tremors, hunched back, lethargy and unkempt appearance. Some survivors demonstrated body weight loss over the 14-day observation period. In the necropsy examination for those animals dying prematurely, gastrointestinal tract abnormalities, intracranial hemorrhages and prominent subcutaneous blood vessels at the application site were noted. **Rat Acute Dermal LD50:** (M) 876 mg/kg, (F) 487 mg/kg; Toxicity Category II; **Study acceptable.** (Kahn, 3/21/86, updated Moore, 1/27/14)

Acute inhalation toxicity, rat **

0037, 276007; "Dicrotophos: 4-Hour Acute Inhalation Toxicity Study in Rats" (Noakes, J.P., Central Toxicology Laboratory, Alderley Park, Macclesfield, Cheshire, UK, Report No. CTL/HR2512/Regulatory/Report, Study No. HR2512, 11/08/2004). 870.1300. Dicrotophos (technical material) (Lot # 403001B, purity = E isomer 87.2%, Z isomer 2.8%) was aerosolized and administered in a nose-only manner under dynamic conditions to 5 Alpk:AP_fSD rats per sex per dose at a dose level (mean gravimetric concentration) of 0.061 mg/l (with a mean MMAD (GSD) of 2.72 (4.00) um) for 4 hours. No mortalities occurred during exposure or during the 14-day observation period. Decreased activity, increased breathing depth, reduced breathing rate, irregular breathing, chromodacryorrhea, reduced foot withdrawal reflex, abnormal respiratory noise, salivation, reduced response to sound, shaking, staining around the nose, and wet fur were observed in both sexes after exposure; hunched posture and increased response to touch were also observed in the females. All of these clinical signs resolved by day 2 except for increased breathing depth and increased response to touch in females which resolved by day 3 and day 5,

respectively. Necropsy revealed no macroscopic abnormalities. LC_{50} (M/F) > 0.061 mg/l. Toxicity Category II. **Acceptable**. (Corlett, 03/06/2014)

Primary eye irritation, rabbit **

299-0018; 45365; "Toxicology of Insecticides: The Acute Oral and Percutaneous Toxicity, Skin and Eye Irritancy and Skin Sensitizing Potential of Bidrin"; (J.B. Price; Shell Research Limited, Sittingbourne Research Centre, Sittingbourne, Kent, ME9, 8AG, England; Doc. No. SBGR.85.266; 12/12/85); The eyes of 6 New Zealand White rabbits were treated by conjunctival instillation with 0.1 ml/eye of Bidrin (Dicrotophos technical) (batch no. 17-1-0-0; Dicrotophos-E content: 88.3%). There was no corneal opacity noted throughout the 14-day observation period. Iritis, grade 0.5 (1/6), was evident at 24 hours post-dose, clearing by 48 hours. Conjunctival redness, grades 2 (3/6) and 1.5 (3/6), were noted at 24 hours post-dose, diminishing to grades 1 (1/6) and 0.5 (4/6) at 7 days, clearing by 14 days. Chemosis, grade 1 (4/6), was evident at 24 hours, clearing by 7 days. Discharge, grade 0.5 (6/6), was noted at 24 hours, clearing by 48 hours. Within 1 hour of dosing, the animals demonstrated constricted pupils and were lying prone, recovering approximately 2.5 hours after dosing. Toxicity Category III; **Study acceptable.** (Kahn, 3/21/86, updated, Moore, 1/27/14)

Primary dermal irritation **

299-0018; 45364; "Toxicology of Insecticides: The Acute Oral and Percutaneous Toxicity, Skin and Eye Irritancy and Skin Sensitizing Potential of Bidrin"; (J.B. Price; Shell Research Limited, Sittingbourne Research Centre, Sittingbourne, Kent, ME9, 8AG, England; Doc. No. SBGR.85.266; 12/12/85); The skin of 6 New Zealand White rabbits was exposed to 0.5 ml/site, one site/animal of Bidrin (Dicrotophos technical) (batch no. 17-1-0-0; Dicrotophos-E content: 88.3%) for 4 hours under a semi-occlusive patch. No erythema or edema were noted throughout the 7-day observation period. Toxicity Category IV; **Study acceptable.** (Kahn, 3/21/86, updated, Moore, 1/27/14).

Dermal sensitization **

299-0018; 45366; "Toxicology of Insecticides: The Acute Oral and Percutaneous Toxicity, Skin and Eye Irritancy and Skin Sensitizing Potential of Bidrin"; (J.B. Price; Shell Research Limited, Sittingbourne Research Centre, Sittingbourne, Kent, ME9, 8AG, England; Doc. No. SBGR.85.266; 12/12/85); Twenty Dunkin-Hartley guinea pigs received a total of 6 intradermal injections of 0.1 ml each, 2 each of Freund's Complete Adjuvant: distilled water (1:1), 0.5% (w/v) dilution of Bidrin (Dicrotophos technical) (batch no. 17-1-0-0; Dicrotophos-E content: 88.3%) in water, and a 0.5% dilution of the test material in a 50:50 mixture of Freund's Complete Adjuvant and water on day 0 of induction. On day 7, the skin of the treated animals was exposed to a filter paper saturated with 0.3 ml of the undiluted test material for 48 hours under an occlusive wrap as the second induction treatment. Ten control animals were treated in the same manner except that the test material was not included in the dosing regimen. Two weeks after the topical induction application, the skin of each of the animals was exposed to a filter paper saturated with 0.1 ml of the undiluted test material for 24 hours under an occlusive wrap. In the challenge, thirteen of the 20 induced animals demonstrated a positive response at 24 hours post-exposure, diminishing to 12 animals at 48 hours. No response was noted for the control animals. The test material is a dermal sensitizer in accordance with the Guinea Pig Maximization Test. The positive control was functional. **Study acceptable.** (Kahn, 3/21/86, updated, Moore, 1/27/14)

SUBCHRONIC STUDIES

Oral toxicity, rat: (No standard rat subchronic, but see 90-day neurotoxicity, below)

Study not submitted.

Oral toxicity, non-rodent:

Study not submitted.

Dermal toxicity, 21/28-day or 90-day: ** † (flagged for brain AChE inhibition)

****299-0060; 280092**; "Dicrotophos: 21/28 Day Dermal Toxicity Study in the Rat"; (J.P. Noakes; Central Toxicology Laboratory, Alderley Park, Macclesfield, Cheshire, UK SK10 4TJ; Study No. LR0588; 2/14/01); The skin of 15 Crl:CD rats/sex/group was treated with 0 (deionized water), 2, 5, 10 or 80 mg/kg/day of Dicrotophos technical (batch no. 403001B; purity: 87.6%) for 6 hours/day for 21 days over a 28-day period. Five of the animals/sex/group were identified as a satellite cohort in which cholinesterase activity was assayed in the brain, red blood cell and plasma at the conclusion of the treatment period. One control female, one female in the 2 mg/kg group, one male in the 5 mg/kg group and one male and four females in the 80 mg/kg group were found dead between study 18 and 21. The report author did not attribute the deaths to treatment because 7 of the 8 deaths occurred at a time when the animals had not been dosed but had been bandaged. The deaths were attributed to poor bandaging. In the clinical observations, an increasing incidence of erythema was noted for the females in all of the treatment groups in a dose-related manner. This effect was not noted for the males. There was no treatment-related effect upon the mean body weights of the animals in the main study. However, the males in the 80 mg/kg treatment of the satellite cohort demonstrated lower mean body weights over the course of the study. There was no treatment-related effect upon food consumption of the main study group. Ophthalmological examination did not reveal any treatment-related effects. There were no treatment-related effects noted in the FOB and motor activity assessment. None of the hematology parameters were affected by the treatment. No treatment-related effects were evident in the clinical chemistry assessment. Cholinesterase activity was reduced in the brains of both sexes in the 10 and 80 m/kg treatment groups (>25% reduction) ($p<0.01$ or 0.05). Similar decrements in red blood cell and plasma activity levels were noted as well. The absolute and/or relative organ weights were not affected by the treatment. There were no treatment-related lesions noted in the histopathological examination. **Possible adverse effect:** significant reduction in brain cholinesterase activity. **Rat 21/28 Day Repeated Dosing Dermal Toxicity NOEL:** (M/F) 5 mg/kg/day (based upon the significant reduction in brain cholinesterase activity noted in both sexes of the 10 mg/kg treatment group); **Study acceptable.** (Moore, 9/19/14) not submitted.

**299-0061; 280093 This is an exact duplicate of 299-0060; 280092, above.

Inhalation toxicity, 28-day to 90-day: (N/A) † (flagged for brain AChE inhibition)

299-0040; 276563; "Dicrotophos Technical: Toxicity Study by Snout-Only Inhalation Administration to CD Rats for 4 Weeks"; (J. A. Blair; Huntingdon Life Sciences Ltd., Alconbury, Huntingdon, Cambridgeshire, PE28 4HS, England; Project ID No. BDG0002; 6/17/10); Ten Crl:CD (SD) rats/sex/group were exposed nose-only to 0, 0.097, 0.73, or 2.9 µg/l

(analytical) of Dicrotophos technical (batch no. GB101309-01; purity: 88.9%) for 6 hours/day, 5 days/week for 4 weeks. The exposure atmosphere consisted of both a particulate and a vapor phase with 90 to 99% of the test material was either vapor or a particle size less than 7 µm. No deaths occurred during the study. The mean body weights and food consumption were not affected by the treatment. In the hematological evaluation, the mean percentage of reticulocytes was reduced for the males in the 2.9 µg/l exposure group ($p<0.05$). No apparent treatment-related effects were noted for the clinical chemistry parameters. Red blood cell cholinesterase (AChE) activity was reduced for both sexes in the 0.73 and 2.9 µg/l exposure groups ($p<0.01$). Brain AChE activity was reduced for both sexes in the 0.73 and 2.9 µg/l exposure groups and for the females in the 0.097 µg/l exposure group ($p<0.05$ or 0.01). There was no treatment-related effect upon the mean organ weights. Atrophy of the seminiferous tubules in the testes of males in the 2.9 µg/l exposure group was noted (0: 0/10 vs. 2.9: 2/10). **Possible adverse effect:** significant reduction in brain acetylcholinesterase activity; **Rat 28-Day Inhalation Toxicity NOEL:** (M) 0.097 µg/l (based upon significant reduction in AChE activity in the brain of the 0.73 µg/l exposure group; (F) < 0.097 µg/l (based upon the significant reduction in AChE activity in the brain of the 0.097 µg/l exposure group); **Study supplemental** (Non-guideline study). (Moore, 8/19/14)

CHRONIC STUDIES

Combined Chronic and Oncogenicity, rat ** † (flagged for brain AChE inhibition)

**** 299-0028; 273372**; "Dicrotophos: Two Year Dietary Toxicity and Oncogenicity Study in Rats"; (S.L. Allen; Central Toxicology Laboratory, Alderley Park, Macclesfield, Cheshire, UK; Study No. PR0986; 2/23/98); Fifty two Alpk:AP_fSD rats/sex/group received 0, 0.5, 5.0 or 25 ppm of Dicrotophos technical (batch no. 403001 B; purity: 87.65% (E isomer)) in the diet for up to 105 weeks ((M) 0, 0.02, 0.25, 1.42 mg/kg/day, (F) 0, 0.03, 0.32, 1.74 mg/kg/day). A satellite cohort of 12 animals/sex/group received the test material in the diet for up to 53 weeks. An additional 16 animals/sex/group were treated for up to 105 weeks and were utilized for the measurement of plasma, red blood cell and brain cholinesterase (ChE) activities at the termination of the study. Eight additional animals/sex/group were treated for 53 weeks and plasma, red blood cell and brain ChE activities were measured at that time. The males in the 25 ppm group demonstrated aggressive behavior, irregular breathing, involuntary shaking of the limbs, urine staining, and hunched posture. The females in the 25 ppm group demonstrated an increased incidence of irregular breathing, involuntary shaking of the limbs, hunched posture, abnormal respiratory noise and piloerection. The females in both the 5 and 25 ppm groups exhibited an increased incidence of urine staining. The survival of the 25 ppm males was so affected by the treatment that surviving animals in that group were euthanized during weeks 95 to 97. The males in the 5.0 ppm group also demonstrated reduced survival such that the remaining groups were euthanized during weeks 99 and 100. The number of females in the 25 ppm group which survived to week 105 was only 29% as well. The mean body weight of the 25 ppm males was lower than that of the control group throughout the study. The 25 ppm females experienced a lower mean body weight in comparison to the controls during the first weeks of the study, recovering thereafter. The mean food consumption for both sexes in the 25 ppm group was less than that of the control group during the first month of the study. Thereafter, food consumption did not appear to be affected by the treatment. Although certain of the

hematological and clinical chemical parameters demonstrated statistically significant differences between the 25 ppm and control groups, there was no consistent effect upon these parameters which exhibited a physiologically significant response. In the urinalysis there was a consistent reduction of the volume and increase in the specific gravity of the urine samples collected from both sexes in the 25 ppm group in comparison to the control group over the course of the study. In the necropsy examination, there was no treatment-related effect upon organ weights. Increased incidences of focal atrophy/degeneration of the acinar epithelium of the Harderian gland and aspiration pneumonia were noted for the females in the 25 ppm group. In the cholinesterase assay, significant reduction in brain, plasma and red blood cell ChE activities was noted for both sexes in the 0.5 ppm group. This result is pertinent because the activities of the latter two ChEs are monitored in the field in an effort to provide surveillance for agricultural workers. This monitoring effort is considered to be health protective because generally the activities of these two cholinesterases are reduced at a concentration which is much lower than the level at which brain cholinesterase is affected. However in this instance that is not the situation. The workers could possibly suffer significant reduction of brain ChE activity before their plasma and/or red blood cell ChE activity levels are sufficiently reduced to warrant the worker's removal from the field; **Possible adverse effect:** significant reduction of brain ChE activity; **Rat Chronic Dietary Toxicity NOEL:** (M/F) < 0.5 ppm ((M) <0.02 mg/kg/day, (F) <0.03 mg/kg/day) (based upon the reduced brain cholinesterase activity of both sexes in the 0.5 ppm group); no oncogenicity was evident. **Study acceptable.** (Moore, 10/10/13)

299-016 036509 "Bidrin: Safety evaluation by a chronic feeding study in the rat for two years," (final report), Howard, D. J., Donoso, J., and Johnston, C. D., Woodard Research Corporation, 9/21/1967. This study employed only 25 rats/sex in treated groups (40/sex in controls). Rats were of unknown strain obtained from Charles River Laboratories, maintained for up to 2 years. The study was hampered by respiratory disease. A high percentage of decedents had substantial autolysis of tissues. No increases in tumors were indicated. Given the availability of a contemporary acceptable combined rat chronic/oncogenicity study, there is no reason to pursue this older study further. Aldous, 11/26/14 (no DPR worksheet).

Chronic, dog ** † (flagged for reduced brain AChE activity)

299-0023, -0055; 273356, 276580; "Dicrotophos: 1-Year Oral Toxicity Study in Dogs"; (S.A. Horner; Central Toxicology Laboratory, Alderley Park, Macclesfield, Cheshire, UK SK10 4TJ; Study No. PD1008; 6/27/97); Four beagle dogs/sex/group were scheduled to be dosed via capsule with 0, 0.025, 0.1 or 1.0 mg/kg/day of Dicrotophos technical (batch no. 403001 B; purity: 87.65%, dosing was adjusted for the purity of the test material) for one year. After 13 weeks, treatment of the high dose level was discontinued for a week, and then resumed at 0.5 mg/kg/day for the remainder of the study. All of the animals survived to the termination of the study. The mean body weights of the 0.1 and 0.5 mg/kg females were less than the control group by the termination of the study ($p<0.05$). There was no apparent treatment-related effect upon the food consumption of the treated animals. Clinical signs included salivation by the females in the 1.0/0.5 mg/kg treatment group. The females in both the 0.1 and 1.0/0.5 mg/kg groups also demonstrated a markedly increased incidence of salivation at the time of dosing. An increased incidence of fluid feces was noted for both sexes in the 1.0/0.5 mg/kg treatment group, particularly during the 1st 13 weeks when they were being treated with 1.0 mg/kg/day. Regurgitation was observed for both sexes in the 1.0/0.5 mg/kg group during week 13. The

hematology evaluation and urinalysis did not reveal any treatment-related effects. In the clinical chemistry evaluation, the serum albumin and calcium levels for both sexes in the 1.0/0.5 mg/kg treatment group were lower than the control values at various times during the study. The serum cholesterol level for the females in the high dose group was also less than that of the control group throughout the treatment period. The plasma cholinesterase (ChE) activities for both sexes in the 0.025 mg/kg treatment group and above were reduced in a treatment-related manner in comparison to the control group activity ($p<0.01$). The red blood cell ChE activities of both sexes in the 1.0/0.5 mg/kg group and the males in the 0.1 mg/kg group were less than that of the control group ($p<0.05$ or 0.01). The brain ChE activities of both sexes in the 1.0/0.5 mg/kg group and the females in the 0.1 mg/kg group were less than the control group value ($p<0.05$ or 0.01). In the necropsy examination, there was no treatment- related effect on the mean organ weights. The histopathological examination did not reveal any treatment-related lesions **Possible adverse effect:** significant reduction in brain ChE activity. **Dog Chronic Oral Toxicity NOEL:** (M/F) <0.025 mg/kg/day (based upon the significant reduction in plasma cholinesterase activity for both sexes in the 0.025 mg/kg treatment group); Previously the study was unacceptable, possibly upgradeable with the submission detailing how the ophthalmological examination was performed; the information provided in record no. 276580 was sufficient to document that the ophthalmological examination was performed; **Study acceptable**. (Moore, 8/28/14)

299-16 036510 "Bidrin: Safety evaluation by a chronic feeding study in the dog for two years," (final report), Johnston, C. D., Thompson, W. M., and Donoso, J.; Woodard Research Corporation, 9/28/1967. This older study involved 3 beagle dogs/sex/group at 0. 16, 1.6, or 16 ppm dicrotophos for 2 years, or 2 dogs/sex at 100 ppm dicrotophos for one year. Investigators reported "fairly consistent salivation, soft stools, and/or tremors in the 100-ppm beagles," with occasional instances of these findings at lower dose levels. Those results of the 100 ppm group may be of interest, because this dose was out of the range of levels used in the accepted study above. Given the availability of a more recent guideline chronic dog study, there is no reason to pursue results of this older study further. Aldous, 11/26/14 (no DPR worksheet).

Oncogenicity, rat (see Combined, above)

See Chronic Toxicity, rat above.

Oncogenicity, mouse ** † (flagged for thyroid adenomas)

**** 299-0024; 273357**; "Dicrotophos: Two Year Oncogenicity Study in Mice"; (G.M. Milburn; Central Toxicology Laboratory, Alderley Park, Macclesfield, Cheshire, UK; Study No. PM0992; 1/7/98); Fifty five C57BL/10J_fCD-1 mice/sex/group received 0, 2, 10 or 50 ppm of Dicrotophos technical (batch no. 403001 B; purity: 87.65%) in the diet for up to 105 weeks ((M) 0, 0.22, 1.12, 6.42 mg/kg/day, (F) 0, 1.58, 9.06 mg/kg/day). The survival of the females in the 50 ppm group was reduced to such an extent that they were euthanized during week 101. The mean body weights of both sexes in the 50 ppm group were less than those of the control group during the first several months of treatment. Thereafter the effect was no longer evident. Food consumption for these animals was less than that of the control week during the first week of the study. No treatment-related effect was apparent thereafter. There were no apparent treatment-related effects noted in the ophthalmoscopic examination. The hematology evaluation did not

reveal any treatment-related effects on the differential white blood counts or the other hematological parameters. In the histopathological examination, there was a treatment-related increase in renal tubular vacuolation for the 50 ppm males in terms of incidence and severity of the lesion in comparison to the controls (0: 23/55 vs. 50: 39/55). The incidence of follicular cell adenoma was also noted in the thyroid glands of these animals (0: 0/54 vs. 50: 5/49). **Possible adverse effect:** follicular cell adenoma in the thyroid gland. **Mouse Chronic Dietary NOEL:** 10 ppm ((M) 1.12 mg/kg/day, (F) 1.58 mg/kg/day) (based upon the initial reduction in body weight of both sexes, the incidence of tubular vacuolation in the kidneys of the 50 ppm males and the reduced survival of the females in the 50 ppm group); **oncogenicity:** follicular cell adenomas in the thyroid gland. **Study acceptable.** (Moore, 9/25/13)

GENOTOXICITY

Bacterial Reverse Mutation Assay **

** 299-0030; 273375; "*Salmonella* Plate Incorporation Mutagenicity Assay (Ames Test) with a Confirmatory Assay"; (R.H.C. San, M.K. Wyman; Microbiological Associates, Inc., Bethesda and Rockville, MD; Study No. G94AW39.501001; 12/2/94); *S. typhimurium* strains TA98, TA100, TA1535, TA1537 and TA1538 were treated with Dicrotophos technical (batch no. 403001B; purity: 87.65%) at concentrations ranging from 100 to 5000 µg/plate under conditions of (+/)- activation, using the plate incorporation method, for 48 to 72 hours at 37° C in two trials. Each treatment level was plated in triplicate. An Aroclor 1254-induced rat liver S9 fraction was used to metabolize the test material. There was no apparent treatment-related increase in the incidence of reverse mutations in any of the strains under conditions of (+/-)-activation. **No adverse effect.** The positive controls were functional. **Study acceptable.** (Moore, 10/16/13)

299-17 036516 Hunter, C. G., "The mutagenic effect of organophosphate insecticides on *Escherichia coli*, Aug. 1971. This report gives an account of testing several OP pesticides with a tryptophan-dependent strain of E. coli. There is nothing to review in this short report except a summary table asserting that all OP pesticides tested (including Bidrin) were negative, whereas several positive controls were positive. No DPR worksheet. Aldous, 12/1/14.

In Vitro Mammalian Cell Assay ** † (positive mouse lymphoma assay)

**** 299-0030; 273376**; "L5178Y/TK$^{+/-}$ Mouse Lymphoma Mutagenesis Assay with a Confirmatory Assay"; (R.H.C. San, J.J. Clarke; Microbiological Associates, Inc., Rockville, MD; Study No. G94AW39.702001; 1/16/95); Mouse lymphoma L5178Y cells (clone 3.7.2C (TK$^{+/-}$)) were treated with Dicrotophos technical (batch no. 403001B; purity: 87.65%) at concentrations ranging from 100 to 3000 µg/ml under conditions of activation and non-activation for 4 hours at 37° C. Two independent trials were performed with 2 replicates per treatment. An Aroclor 1254-induced rat liver S9 fraction was used to activate the test material. Cell viability and mutation frequency were determined and compared to the solvent control level. There was a treatment-related increase in the mutation frequency above that of the solvent control under conditions of both activation and non-activation. **Adverse effect indicated.** The positive controls were functional. **Study acceptable.** (Moore, 10/17/13)

In Vivo Cytogenetics Assay **

** 299-0030; 273374; "Micronucleus Cytogenetic Assay in Mice"; (D.L. Putnam, R.R. Young; Microbiological Associates, Inc., Bethesda and Rockville, MD; Study No. G94AW39.122;

11/15/94); Five ICR mice/sex/group/time point were dosed by intraperitoneal injection (ip) with 0 (distilled water), 1.7, 3.3, or 6.6 mg/kg of Dicrotophos technical (batch no. 403001B; purity: 87.65%). For the positive control, five mice/sex were dosed ip with 40 mg/kg of cyclophosphamide. Treated animals were euthanized at 24, 48 and 72 hours after dosing. The animals which were treated with the positive control were euthanized at 24 hours post dose. Femoral bone marrow was harvested and evaluated for the presence of micronuclei in polychromatic erythrocytes (PCE). One thousand polychromatic erythrocytes were evaluated per animal. One male and three females in the 6.6 mg/kg group died and were replaced. Treatment with the test material did not result in an increase in the number of micronuclei per 1000 PCE's. **No adverse effect indicated.** The positive control was functional. **Study acceptable.** (Moore, 10/16/13)

299-017 036517 Dean, B. J. and K. Senner, "Chromosome studies on bone marrow cells of mice after a single oral dose of Bidrin," Tunstall Laboratory, Dec. 1973. In a study which pre-dated current guidelines, and which had no QA oversight and no concurrent positive controls, Bidrin was administered to male and female mice at 0, 5, or 10 mg/kg at 8 hrs or 24 hrs prior to sacrifice and examination of bone marrow cells. There was no increase in chromatid gaps or breaks, and no effect on polyploidy associated with Bidrin treatment. No adverse effects are indicated. Supplementary data: no DPR worksheet. Aldous, 12/1/14.

Miscellaneous Genotoxicity Assays (not classifiable with current guidelines)

299-017 036515 Doak, S. and C. Whitebread, "Toxicity studies with Bidrin in the host-mediated assay and with microorganisms *in vitro*," Tunstall Laboratory, July 1974. This brief (7-page) report describes direct (buffered solution) and host mediated (mouse ip injection of cells) exposures of a double auxotrophic strain of *Saccharomyces cerevisiae* to dicrotophos at a range of dose levels. The host-mediated trails were negative. Bidrin was weakly positive in some direct trials at 5 to 10 µg/ml, negative at 20 µg/ml, and clearly positive at 50 µg/ml (5% solution). Thus study indicates a "possible adverse effect," although reliably so only at very high dose levels. This *Saccharomyces cerevisiae* test system is no longer commonly used. Since there is an accepted positive eukaryotic cell gene mutation assay already (Record No. 273376), and since this study pre-dates current guidelines, there is no worksheet for this report. Aldous, Dec. 1, 2014.

299-017 036518 Dean, B. J., "Dominant lethal in male mice after single or repeated oral dosing with Bidrin," Tunstall Laboratory, Nov. 1974. Typically 12 male mice/group were dosed once with Bidrin at 5 or 10 mg/kg in Trial 1, or in Trial 2 either with a single dose of 10 mg/kg Bidrin, or with 1 or 2 mg/kg/day for 5 consecutive days. Twenty-four untreated controls were used in each trial, and MMS was used as a positive control in Trial 1 only. Bidrin did not cause consistent effects on percentage pregnancies in groups, or on total implants per pregnant female, or (most importantly) on early fetal deaths. This study pre-dates current guidelines. As this is a negative study, there is no DPR worksheet for this report. Aldous, Dec. 1, 2014.

REPRODUCTIVE TOXICITY, RAT ** † (flagged for excessive pup mortality)

**** 299-0029; 273373**; "Dicrotophos: Multigeneration Study in the Rat"; (M.E. Moxon; Central Toxicology Laboratory, Alderley Park, Macclesfield, Cheshire, UK; Study No. RR0689; 3/18/97); In the F0 generation, twenty six Wistar rats/sex/group were scheduled to receive 0, 0.5, 5.0 or 25 ppm of Dicrotophos technical (batch no. 403001 B; purity: 87.65% (E isomer)) in the diet for 10 weeks of premating, during mating, and 3 weeks of gestation and 4 weeks of lactation. Due to the high loss of offspring in the 25 ppm group, the treatment was reduced to 10 ppm from lactation day 8 through 29. A second mating (designated F1B) of the F0 generation was instituted in which the parents in the high dose group were treated with 15 ppm of the test material from mating through the end of the lactation period. At the time of the selection of the F1 adults from the F1B litters, the concentration was readjusted to 10 ppm for the remainder of their treatment (i.e., 10-week premating, mating, gestation and lactation periods) ((M) 0, (0.5 ppm) 0.05, (5.0 ppm) 0.49 to 0.56, (25 ppm) 2.53, (10 ppm) 1.15 mg/kg/day, (F) (0.5 ppm) premating: 0.05 to 0.06, gestation: 0.04, lactation: 0.11 to 0.12 mg/kg/day, (5.0 ppm) premating: 0.53 to 0.59, gestation: 0.42 to 0.44, lactation: 1.02 to 1.15 mg/kg/day, (25 ppm) premating: 2.79 mg/kg/day, (10 ppm) premating: 1.25, gestation: 0.89, lactation: 2.08 mg/kg/day, (15 ppm) gestation: 1.29, lactation: 2.46 mg/kg/day). There was no apparent effect upon the survival of the parental generations. Involuntary shaking of the limbs was noted for both sexes in the 25 ppm treatment group (F0 generation) during the first weeks of the premating period. The mean body weights of the adults in the 5.0 ppm and above treatment levels were less than the control body weights during the premating and lactation time period (NS, $p<0.05$ or 0.01). The mean body weights during the gestation periods of both generations were not affected by the treatment. The mean food consumption of both sexes in the 25 ppm treatment group was less than that of the control group in the F0 generation during the 1st month of the premating period. Thereafter there was no treatment-related reduction on food consumption until the lactation periods of the F0 generation (10 and 15 ppm treatment groups) and the lactation period of the F1 generation (5.0 and 10 ppm treatment groups). The fertility indices of the dams in the high dose group of the F0 generation (25 and 15 ppm treatment levels) were lower than that of the control group. At a treatment level of 10 ppm for the F1 generation, no effect on fertility was evident. The gestation indices were not affected at any of the treatment levels. Pup viability indices were affected in a treatment-related manner at the 5 ppm treatment level and above for both generations. There was no apparent treatment-related effect upon the pup weights. **Possible adverse effect:** excessive pup mortality; **Parental NOEL:** 0.5 ppm ((M) 0.05 mg/kg/day; (F) 0.05 to 0.06 mg/kg/day) (based upon treatment-related effect upon the body weights of both sexes in the 5.0 ppm treatment group); **Reproductive NOEL:** 10 ppm (1.25 mg/kg/day) (based upon the reduced fertility indices for the 15 ppm treatment group and above); **Developmental NOEL:** 0.5 ppm (0.05 to 0.06 mg/kg/day) (based upon the reduced pup viability noted for the 5.0 ppm treatment groups of both generations); **Study acceptable.** (Moore, 10/15/13)

299-017 036514 "Results of reproduction study of rats fed diets containing Bidrin insecticide over three generations," Eisenlord, G., The Hine Laboratories, Aug. 1965. This 14-page report describes a study in which rats were initially administered 0, 2, 5, 15, or 50 ppm Bidrin. The 50 ppm dose group was discontinued after F1b littering period due to weakness and weight loss in parents, CNS signs such as tremors and incoordination in pups, and high mortality in litters. This study pre-dates current guidelines, and cannot be made acceptable, and is designated as

supplementary data. There is no DPR worksheet, since the accepted study above (Record No. 273373) spanned an effective dose-response range. Aldous, Dec. 1, 2014.

DEVELOPMENTAL TOXICITY

Rat **

** 299-0025; 273358; "Developmental Toxicity of Technical Bidrin Insecticide in Sprague-Dawley Rats"; (D.E. Rodwell; WIL Research Laboratories, Inc., Ashland, OH; Study No. WIL-93006; 6/25/86); Twenty five mated female Sprague-Dawley rats/sex/group were dosed orally by gavage with 0, 0.1, 0.5, 1.0 or 2.0 mg/kg/day of Bidrin technical (dicrotophos); no batch no.; purity: 89.7%) from day 6 through day 15 of gestation. The mean body weight gains of the dams in the 1.0 and 2.0 mg/kg treatment groups were less than that of the control group over the course of the treatment period. The 2.0 mg/kg group exhibited treatment-related clinical signs of teeth gritting, fasciculations, tremors, decreased muscle tone, nasal discharge, signs of diarrhea, urogenital staining and salivation. The 1.0 mg/kg dams also demonstrated the fasciculations. There were no apparent treatment-related effects upon the development of the fetuses. **No adverse effect indicated. Maternal NOEL:** 0.5 mg/kg/day (based upon the clinical signs, lower body weight gain and reduced food consumption noted for the 1.0 mg/kg treatment group); **Developmental NOEL:** 2.0 mg/kg/day (based upon the lack of a treatment-related effect upon the fetuses in the 2.0 mg/kg group); **Study acceptable.** (Moore, 10/8/13)

299-019 047154 This is a duplicate copy of study 299-0025; 273358, above.

Rabbit **

** 299-0026, -0027; 273359, 273360; "Dicrotophos: Prenatal Developmental Toxicity Study in the Rabbit:"; (M.E. Moxon; Central Toxicology Laboratory, Alderley Park, Macclesfield, Cheshire, UK; Study No. RB0865; 4/9/01); Twenty eight mated New Zealand White female rabbits/group were dosed orally by gavage with 0 (vehicle: water), 0.5, 1.0 or 2.0 mg/kg/day of Dicrotophos technical (batch no. 403001 B; purity: 87.65%) from gestation day 5 through gestation day 29. Two does in the 2.0 mg/kg group were euthanized *in extremis* on day 29 due to the severity of their clinical signs. One doe in the 1.0 mg/kg group was euthanized on day 30 following signs of an abortion. Clinical signs for the does in the 2.0 mg/kg treatment group included shaking, hunched posture, subdued behavior, increased breathing rate, abnormal respiratory noise, salivation, mucus in the feces, signs of diarrhea and staining in the genital area. For the does in the 1.0 mg/kg group, mucus was noted in the feces and there were signs of diarrhea. No treatment-related clinical signs were noted for the does in the 0.5 mg/kg group. The mean body weights of the 2.0 mg/kg does were less than the control group values at the initiation of dosing and during the last few days of gestation ($p<0.05$). The mean food consumption of the 1.0 and 2.0 mg/kg treatment groups was less than that of the control group during the last four days of the gestation period ($p<0.01$). The mean weight of the 2.0 mg/kg group fetuses was less than those in the control group ($p<0.01$). **No adverse effect was evident. Maternal NOEL:** 0.5 mg/kg/day (based upon the treatment-related clinical signs noted for the 1.0 mg/kg does); **Developmental NOEL:** 1.0 mg/kg/day (based upon the lower mean body weights noted for the fetuses in the 2.0 mg/kg group); **Study acceptable.** (Moore, 10/1/13)

299-017 036513 "Toxicity studies with Bidrin: Teratological studies in rabbits given Bidrin orally," Tunstall Laboratory, Sittingbourne (presumably Kent, UK). Dix, K. M., A. B. Wilson, and W. V. McCarthy, Study TLGR.0020.73, Aug. 1973. Initially 32 control banded Dutch rabbits, or groups of 16 does administered 1.3 or 4.0 mg/kg/day Dicrotophos on gestation days 6-18, or positive control (16 dams administered 37.5 mg/kg/day thalidomide) were evaluated for developmental toxicity. These dose levels did not cause clear clinical signs. Three of 13 litters in the initial study administered 4 mg/kg/day dicrotophos had visceral abnormalities, prompting a repeat study. In the second study phase, 36 control does were compared to dicrotophos levels of 18 dosed with 1.3, 4, or (initially) 12 mg/kg/day. The latter dose proved too toxic: 3 of ten 12 mg/kg/day does died. Reduction of the highest dose in the second study phase to 8 mg/kg/day still found several clinical signs in the does, and one additional death. In the second phase, 2/21 control litters had visceral abnormalities, compared to none in dicrotophos groups (1.3, 4, or 8 mg/kg/day, with 12, 13, and 8 litters examined, respectively). Investigators justifiably concluded that dicrotophos was not a developmental toxicant under study conditions. Study pre-dated current guidelines, and lacked features such as QA oversight or dosing solution analysis, so that there is no DPR worksheet. Useful supplementary data. Aldous, Dec. 1, 2014.

NEUROTOXICITY

Acute neurotoxicity, rat ** † (flagged for brain AChE)

**** 299-0032; 273379**; "Dicrotophos: Acute Neurotoxicity Study in Rats"; (N.J. Rattray; Central Toxicology Laboratory, Alderley Park, Macclesfield, Cheshire, UK SK1 0 4TJ; Study No. AR5795; 2/20/95); Ten Wistar rats/sex/group were dosed orally by gavage with 0 (distilled water), 0.5, 5 or 10 mg/kg of Dicrotophos technical (batch no. 403001B; purity: 87.65%). A satellite cohort of 10 animals/sex/group were dosed in the same manner. Five animals/sex/group/time point were euthanized at 3 hours or 8 days post-dose. Brain, red blood cell and plasma cholinesterase (ChE) activities were assayed. One male and six females in the 10 mg/kg group died within 3 hours of dosing. Clinical signs included decreased activity, ataxia, chromodacryorrhea, flaccidity, reduced foot withdrawal reflex, decreased pupillary response to light, salivation, shaking, sides pinched in, stains around mouth and nose, signs of urinary incontinence, tip toe gait and upward curvature of the spine. Most of these signs were demonstrated by both sexes in the 5 and 10 mg/kg treatment groups and were only evident on the day of dosing. The mean body weights of the 10 mg/kg males were less than those of the control group over the two-week observation period ($p<0.01$). The food consumption of these animals was also less than that of the control group during the first week post-dose. In the time to tail flick test, both sexes in the 5 and 10 mg/kg groups demonstrated a prolonged response time interval for the test on the day of dosing. In the grip strength assessment, the fore- and/or hindlimb grip strengths of both sexes in the 5 and 10 mg/kg groups were lower than those of the control group on the day of dosing (NS, $p<0.05$ or 0.01). Likewise, the motor activity of both sexes in the 5 and 10 mg/kg group was less than that of the control group animals on the day of dosing. None of these effects were evident in later functional observational battery or motor activity assessments. There was a significant reduction in brain cholinesterase activity for the animals in the 0.5 mg/kg and above on the day of dosing ($p<0.01$). The effect persisted in the 10 mg/kg males through the 1st week post-dose. Red blood cell and plasma cholinesterase activity levels for all of the treatment groups were also significantly reduced in comparison to the control

levels on the day of dosing. An effect was still evident on the red blood cell ChE activity of both sexes in the 10 mg/kg group at 1 week post-dose. The significant reduction of brain ChE activity at treatment levels for which plasma and red blood cell ChE activity levels are only marginally affected presents a major concern in regard to monitoring the activity levels of these two enzymes in worker safety programs. There was no apparent treatment-related effect noted in the necropsy or histopathological examinations. **Possible adverse effect:** reduced cholinesterase activity in the brain. **ACUTE NEUROTOXICITY NOEL**: (M/F) <0.5 mg/kg (based upon the reduced brain cholinesterase activity noted for both sexes in the 0.5 mg/kg treatment group); **Study acceptable.** (Moore, 10/23/13)

90-day neurotoxicity, rat ** † (flagged for AChE inhibition)

**** 299-0041; 276564**; "Dicrotophos: Subchronic Neurotoxicity Study in Rats"; (S.A. Horner; Zeneca Central Toxicology Laboratory, Alderley Park, Macclesfield, Cheshire, UK; Report No. CTL/P/4692; 11/6/95); Twelve Alpk:AP_fSD rats/sex/group received 0, 0.5, 5 or 25 ppm of Dicrotophos technical (batch no. 403001B; purity: 87.65%) in the diet for 13 weeks ((M) 0, 0.04, 0.39, 2.03 mg/kg/day, (F) 0, 0.04, 0.45, 2.38 mg/kg/day). Two satellite cohorts of 6 animals/sex/group/cohort were treated in the same manner for 5 and 9 weeks, respectively. At those times, the animals were euthanized and plasma, red blood cell and brain cholinesterase (ChE) activities were assayed. The mean body weights and food consumption of both sexes in the 25 ppm group were less than the control values during the 1st weeks of the study ($p<0.05$ or 0.01). In the FOB, a decreased pupillary response was noted for 5 of 17 males and 2 of 18 females in the 25 ppm group at week 9. This was the only time point for which this effect was remarkable. The forelimb and hindlimb grip strength of the 25 ppm females was minimally reduced at week 9 ($p<0.01$ or 0.5). This effect was less apparent by week 14. Motor activity of both sexes in the 25 ppm group was reduced at week 9 and persisted through week 14 (NS, $p<0.01$ or 0.05). The ChE activity in the brain was reduced in both sexes of the 0.5 ppm treatment group and above ($p<0.01$ or 0.05). The plasma and red blood cell ChE activities were likewise reduced for both sexes in the 0.5 ppm treatment group at various time points during the study ($p<0.01$ or 0.05). There were no treatment-related lesions noted in the necropsy or histopathological evaluations. **Possible adverse effect:** significant reduction in brain ChE activity**. Rat Subchronic Neurotoxicity NOEL:** (M/F) < 0.5 ppm (0.04 mg/kg/day) (based upon the reduced cholinesterase activity in the brain of both sexes in the 0.5 ppm treatment group). **Study acceptable.** (Moore, 8/26/14) Another copy of this report was submitted in a subsequent submission package and under a different record number (Document No. 299-0064, Record No. 280958). The latter copy was evaluated by Aldous on 11/20/14. Conclusions by the two DPR reviewers were comparable, so only the above 1-liner is needed in this Summary.

Developmental neurotoxicity, rat **

** 299-0031; 273377; "Dicrotophos: Developmental Neurotoxicity Study in Rats"; (A. Brammer; Central Toxicology Laboratory, Alderley Park, Macclesfield, Cheshire, UK SK1 0 4TJ; Study No. RR0884; 10/24/03); Thirty time-mated female Wistar rats/group were dosed orally by gavage with 0 (vehicle: deionized water), 0.01, 0.05 or 0.4 mg/kg/day of Dicrotophos technical (batch no. 403001B; purity: 87.65%) from day 7 gestation through day 7 *post-partum*. The pups in the F1 generation were dosed orally by gavage from day 8 through day 22 *post-partum*. A functional observational battery (FOB) was performed on the F0 dams on days 10 and 17 of gestation and on days 2 and 9 of lactation. For the F1 generation, the FOB was

performed on 10 pups/sex/group (one male or female from each litter) on *post-partum* days 5, 12, 22, 36, 46 and 61 in the same manner as it was performed with the dams. Motor activity was measured for one male and one female selected from each litter on days 14, 18, 22 and 60. The auditory startle response was assessed for one male and one female per litter on days 23 and 61and the learning and memory was assessed using one male and one female from each litter on days 21 and 24 and 59 and 62. Two F0 females in the control group were euthanized due to parturition difficulties. There was no treatment-related effect upon the mean body weights of the F0 generation dams. The reproductive performance of the dams was not affected by the treatment. For the dams, no treatment-related clinical signs were evident in the FOBs performed over the course of the study. The treatment did not affect the mean body weights of the F1 generation offspring. The time to preputial separation or vaginal opening was not affected by the treatment. The F1 animals did not exhibit any treatment-related clinical signs in the FOBs or motor activity measurements performed. The startle response test did not demonstrate any apparent developmental deficits. There was no treatment-related effect in the learning and memory tests. In the necropsy examination, although the absolute brain weights of the pups in the 0.4 mg/kg group were statistically greater than those of the control group at either 12 or 63 days *post-partum*, there was no effect on the relative brain weights. No treatment-related lesions were noted in the histopathological examination. In the brain morphometric analysis, although certain of the measurements for the F1 offspring in the 0.4 mg/kg group were significantly different from that of the control group, no consistent effect on the brain structure was evident. **No adverse effect indicated. Maternal NOEL:** 0.4 mg/kg/day) (based upon the lack of treatment-related effects on the dams in the 0.5 mg/kg treatment group); **Developmental NOEL:** 0.4 mg/kg/day (based upon the lack of a treatment-related effect on the development of the pups in the 0.4 mg/kg treatment group); **Developmental Neurotoxicity NOEL:** 0.4 mg/kg/day (based upon the lack of the treatment-related effect on the pups in the 0.4 mg/kg group); **Study acceptable.** (Moore, 10/18/13)

In a preliminary developmental neurotoxicity study (study no. RR883), reported in vol. no. 299-0031 under record no. 273377, dams experienced significant reduction in cholinesterase (ChE) activity in the RBC and brain of the dams at treatment levels of 0.05, 0.2 and 1.0 mg/kg/day. Fetal RBC and brain ChE activities were reduced on gestation day 22 at the 0.2 and 1.0 mg/kg/day treatment levels. The offspring did not demonstrate any ChE inhibition on lactation days 8, 15 or 22. In a second preliminary study (study no. KR1491), pre-weanling rats 12 days old or young adults 42 days old were dosed orally by gavage for 7 days with 0.008, 0.02, 0.08 or 0.4 mg/kg/day. Reduced brain and RBC ChE activities were noted for the pre-weanlings and young adults treated with 0.4 mg/kg/day. The pre-weanlings also demonstrated reduced RBC ChE activity at 0.08 mg/kg/day. Based on these results, 0.01, 0.05 and 0.4 mg/kg/day were selected as the treatment levels for the guideline study.

299-0031; 273378 This is an analysis of brain morphometry, sent as a response to a U.S. EPA request. It is a few pages in length, and should be considered part of Record No. 273377.

Delayed neurotoxicity, hen **

** 299-0033; 273380; “Dicrotophos: A Delayed Neurotoxicity Study in Laying Hens Phase II-Acute Neurotoxicity Assessment”; (L.T. Frey, J.B. Beavers, K.H. Martin, M.J. Jaber; Wildlife International, Ltd., Easton, MD; Project No. 246-112; 7/7/00); Twenty Single comb, white

leghorn hens were dosed orally by intubation with 11 mg/kg of Dicrotophos technical (lot no. 8070030051; E isomer: 87.2%, Z isomer: 6.2%). Twelve hens/group were dosed in the same manner with either 0 (reverse osmosis water) or 600 mg/kg of tri-orthocresyl phosphate (TOCP) in corn oil. The hens treated with dicrotophos were also given intramuscular injections of atropine (0.5 mg/kg) and 2-PAM (50 mg/kg) immediately prior to dosing, once later in the day, 3 times on day 1 and three additional injections of atropine on day 2. The hens in the dicrotophos treatment group demonstrated acute symptoms of toxicity; lethargy, loss of coordination, wing droop, reduced reaction to external stimuli, lower limb weakness and depression. These signs were first noted on day 1 and continued in at least one bird until day 8. Thereafter, no signs were evident. These hens demonstrated a loss in body weight during the first week post-dose, thereafter regaining the weight. The food consumption of these birds was reduced for the first week in comparison to the control group, recovering to the control level for the remainder of the study. In the ataxia assessment, the dicrotophos-treated birds demonstrated some acutely toxic effects during the first week, largely recovering during the second week. The positive control cohort, the TOCP-treated birds, did not demonstrate the delayed neurotoxic deficit as expected. Neurotoxic esterase (NTE) activity in the brain and spinal cord of the dicrotophos-treated hens was 92 and 75% of the control values, respectively, at 2 days post-dose. The TOCP- treated hens demonstrated activity levels of 9 and 13% of the control values for the brain and spinal cord, respectively. The brain acetyl- cholinesterase activity in the dicrotophos-treated hens was only 16% that of the control group in contrast to that of the TOCP-treated birds which was 79% of control. The histopathological evaluation did not reveal any treatment-related lesions in either the dicrotophos- or TOCP-treated hens. These results confirmed the lack of treatment-related effects in the ataxia assessment. **No adverse effect indicated.** The positive control was not fully functional, no delayed neuropathy was manifested. Despite this result, there was sufficient information to substantiate that dicrotophos is not a delayed neurotoxicant. **Study acceptable.** (Moore, 10/24/13).

299-0034; 273381; "Dicrotophos: A Delayed Neurotoxicity Study in Laying Hens Phase I-Acute Oral Toxicity and Evaluation of Atropine and 2-PAM Protection"; (L.T. Frey, J.B. Beavers, K.H. Martin, M.J. Jaber; Wildlife International, Ltd., Easton, MD; Project No. 246-111; 8/19/99); A dose range-finding study was performed in which white leghorn hens were dosed orally by intubation with Dicrotophos technical (lot no. 8070030051, E isomer: 87.2%, Z isomer: 6.2%). In the first phase, five hens/group were dosed with 0 (reverse osmosis water), 3, 5, 7, 9, 11, 15 or 20 mg/kg of the test material and observed for 7 days. The following mortality resulted from the treatment: 0: 0/5, 3: 0/5, 5: 0/5, 7: 0/5, 9: 0/5, 11: 3/5, 15: 5/5, 20: 5/5. In the 2nd phase of the study, 5 hens/group were treated with 11 mg/kg + atropine (5 mg/kg) or 11 mg/kg + atropine (5 mg/kg)+2-PAM (50 mg/kg). In addition, 4 hens/group were treated with 22 mg/kg + atropine (5 mg/kg) or 22 mg/kg + atropine (5 mg/kg)+2-PAM (50 mg/kg). The atropine and 2-PAM were administered by intramuscular injection. Additional injections of atropine and 2-PAM were administered as needed. The hens were observed for 7 days. The following mortality resulted from the treatment: 11 mg/kg + atropine: 3/5, 11 mg/kg + atropine+ 2-PAM: 1/5, 22 mg/kg + atropine: 4/4, 22 mg/kg + atropine + 2-PAM: 4/4. Based on these results, a treatment level of 11 mg/kg was selected for the guideline study. In this study atropine and 2-PAM would be administered in order to protect against the acute neurotoxic effects of dicrotophos. **Study supplemental.** (Moore, 10/24/13)

IMMUNOTOXICITY **

** 299-0035; 273382; "Dicrotophos Technical: 4 Week Dietary Immunotoxicity Study in the Male Han Wistar Rat"; (W. Arrowsmith; Huntingdon Life Sciences Ltd., Alconbury, Huntingdon, Cambridgeshire, PE28 4HS, England; Project ID No. BDG0003; 2/3/11); Ten male Wistar rats/group received 0, 5, 15 or 25 ppm of Dicrotophos technical; batch no. GB101309-01; purity: 88.9% (E-isomer: 85.4%, Z-isomer: 3.5%) in the diet for 4 weeks (0, 0.37, 1.14, 1.91 mg/kg/day). Another 8 males were dosed by intraperitioneal injection with 50 mg/kg of cyclophosphamide in 0.9% saline on day 27 as the positive control group. On day 25, five days before necropsy on day 29, each animal received an iv injection of $2x10^8$ sheep red blood cells (SRBC). SRBC-specific IgM plaques were determined for each animal by incubating a spleen cell suspension preparation with guinea pig complement and SRBC. No deaths occurred during the treatment period. The mean body weight gain of the 25 ppm animals was less than that of the control group over the course of the study ($p<0.01$). Brain and red blood cell cholinesterase activities were reduced in a dose-related manner in all of the treated groups ($p<0.01$). In the necropsy examination, the adjusted spleen weight of the 25 ppm males was greater than that of the control group ($p<0.05$). This greater weight was reflected in the greater numbers of cells/spleen and plaque-forming cells/spleen determined in the plaque forming assay. There was no treatment-related effect evident in the plaque-forming cell assay. **No adverse effect indicated.** The positive control was functional. **Study acceptable.** (Moore, 10/25/13)

ENDOCRINE DISRUPTOR STUDIES

No study submitted nor required at this time.

MECHANISTIC STUDIES (largely acetylcholinesterase inhibition)

299-0067 280961 Moxon, M. E., "Dicrotophos: acute cholinesterase inhibition study in pre-weaning rats," Central Toxicology Laboratory, Alderley Park, Macclesfield, Cheshire, UK, 10/24/03. Laboratory Study # CTL/AR7148/Regulatory/Report. Groups of 5 pups/sex were dosed by gavage once with Dicrotophos Technical, 90.4% purity, Batch 403001B at three ages (PND 8, 15, and 22), and at 5 dose levels (0, 0.1, 0.3, 1, and 5 mg/kg). Pups were killed about 2 hrs after dosing for assays of brain and RBC AChE. All 5 mg/kg pups suffered tremors. Additional characteristic signs of AChE inhibition were seen in 5 mg/kg pups: most evident at PND 15. Clinical signs at lower dose levels were limited to one 1 mg/kg pup with slight tremors. Well-defined and statistically significant brain AChE inhibition dose-responses were observed for both sexes and all ages of pups over the dose range from 0.3 to 5 mg/kg dicrotophos. Also, brain AChE in 0.1 mg/kg pups was slightly below controls, generally also significantly significant. Regardless of sex, well-defined RBC AChE inhibition dose-responses were observed for all ages of pups over the dose range from 0.3 to 5 mg/kg Dicrotophos (statistically significant except for PND 8 females). At PND 15 and PND 22, RBC AChE in 0.1 mg/kg pups was appreciably below controls, generally also significantly significant. In contrast, there was no decline in RBC AChE in PND 8 pups at 0.1 mg/kg. This supplementary study did not seek and did not find a NOEL, however useful dose-response patterns were revealed, so that the study provides valid supplementary data. Aldous, 11/17/14.

299-0068 280962 Brammer, A., "Dicrotophos: acute cholinesterase inhibition study in rats," Central Toxicology Laboratory, Alderley Park, Macclesfield, Cheshire, UK, 4/4/02. Laboratory Study # AR7078. Groups of 5 Alpk:AP_fSD rats/sex/[sacrifice group] were dosed once by gavage with Dicrotophos [87.6% purity, Batch 403001B] at dose levels of 0, 0.1, 0.3, and 5 mg/kg and sacrifice times of 3 hours on day 1, and on days 8 and 15. Prominent clinical signs, all limited to 5 mg/kg rats, included tremors, decreased activity, splayed gait, reduced stability, sides pinched in, spine curved upward, and irregular breathing. All of these signs were limited to the first treatment day. Slightly decreased day 8 body weights for 5 mg/kg males and small food consumption reductions in 5 mg/kg females during week 1 may also have been treatment-related. Day 1 brain AChE activity was reduced in 5 mg/kg males by 74%, with no measurable effect at 0.3 mg/kg. Day 1 brain AChE activity was reduced in 5 mg/kg females by 76%, and there was a 22% reduction at 0.3 mg/kg. There was an equivocal brain AChE activity reduction in 5 mg/kg females at day 8 (18% below concurrent control). Day 1 RBC AChE activities were reduced in dose-related fashion, statistically significantly so in males and females at 0.3 and 5 mg/kg. Percent reductions were 15% and 47%, respectively, in males; and 10% and 39%, respectively, in females. There were no RBC AChE changes at later sacrifice times. NOEL for parameters assessed in this study was thus 0.1 mg/kg. Useful supplementary data. Aldous, 11/18/14.

299-0065 280959 Brammer, A., "Dicrotophos: repeat dose bridging study in rats," Central Toxicology Laboratory, Alderley Park, Macclesfield, Cheshire, UK, 2/18/02. CTL Laboratory Study No. KR1455. Groups of 5 rats/sex/group were dosed by gavage daily for 28 days or 56 days in a study to assess clinical signs and cholinesterase (ChE: brain and RBC) effects of Dicrotophos, 87.6% purity, Batch 403001B. Dose levels were 0 or 0.4 mg/kg/day. Investigators focused on possible accumulated effects, rather than on peak effect after bolus dosing. Rats were examined pre-test and **just before** daily dosing for clinical signs. Necropsy (mainly for brain and RBC sampling) was one day after final dosing respective groups. No clinical signs were evident when examined (nearly 24 hours since the previous day's dose). Body weights were marginally decreased by study termination in both sexes. Brain and RBC ChE activities did not vary by sex, and inhibition did not change significantly between the 4-week and the 8-week treatment regimen. Study provides useful supplementary data, with some deficiencies in the report. Aldous, 11/20/14.

299-0039; 276562; "Dicrotophos: Repeat Dose Cholinesterase Inhibition Study in Rats"; (A. Brammer; Central Toxicology Laboratory, Alderley Park, Macclesfield, Cheshire, UK; Study No. KR1456; 6/24/02); Ten Wistar-derived rats/sex/group were dosed orally by gavage with 0 (vehicle: deionized water), 0.008, 0.02 or 0.4 mg/kg/day of Dicrotophos technical (batch no. 403001B; purity: 87.6%) for 28 days. Five animals/sex/group in the main study were euthanized at the conclusion of dosing and brain and red blood cell acetylcholinesterase (AChE) activities were measured. A recovery cohort of 5 animals/sex/group were maintained treatment-free for an additional 4 weeks. At that time the animals were euthanized and the brain and RBC AChE activities were assayed. No test material-related deaths occurred during the study. There were no apparent treatment-related clinical signs or effects on mean body weight. In the main study group, the brain AChE activity levels of both sexes in the 0.4 mg/kg treatment group and the females in the 0.02 mg/kg group were reduced in comparison to the control group values (NS or $p<0.01$). In the recovery cohort, the female brain AChE activity levels were still reduced for all of the treated groups after 4 weeks. This persistence may have been due to an exceptionally high

control activity level. However, this potential effect bears further evaluation. **Possible adverse effect:** significant reduction in brain AChE activity; **Rat 4-Week Oral Toxicity NOEL:** (M) 0.02 mg/kg/day (based upon reduced brain AChE activity in the 0.4 mg/kg treatment group; (F) 0.008 mg/kg/day (based upon the reduced brain AChE activity in the 0.02 mg/kg treatment group); **Study supplemental.** (Moore, 8/8/14). Another copy of this report was submitted in a subsequent submission package and under a different record number (Document No. 299-0066, Record No. 280960). The latter copy was evaluated by Aldous on 11/20/14. Conclusions by the two DPR reviewers were comparable, so only the above 1-liner is needed in this Summary.

299-0069 280963 Moxon, M. E., "Dicrotophos: repeat dose cholinesterase inhibition study in pre-weaning and young adult rats," Central Toxicology Laboratory, Alderley Park, Macclesfield, Cheshire, UK, 10/24/03. CTL Study # KR1491. Alpk:APfSD rats, 5/sex/group, were dosed by gavage for 7 consecutive days with Dicrotophos [90.4% purity, Batch 403001B] at 0, 0.008, 0.02, 0.08, 0.4, or 1 mg/kg/day. This regimen applies to both pre-weaning and young adults. For pre-weanlings, dosing was PND 12-18. For young adults, dosing was PND 42-48. The primary assessments were of brain and RBC acetylcholinesterase (AChE): in all cases assessed after sacrifice 2 hrs following the last treatment. NOEL = 0.02 mg/kg/day for RBC AChE in pre-weanling rats. The NOEL for brain and RBC AChE in young adult rats is 0.08 mg/kg/day, as is the NOEL for brain AChE in pre-weanling rats. In all cases, inhibition was strong at 0.4 mg/kg/day and above in pre-weaning and in young adult rats, with inhibition typically slightly greater in pre-weaning rats. There were no clinical signs at any dose tested. Useful supplementary data. Aldous, 11/21/14.

299-0062; 280094; "Dicrotophos: 14 Day Dermal Toxicity Study in the Rat with Cholinesterase Determination"; (I.R. Johnson; Central Toxicology Laboratory, Alderley Park, Macclesfield, Cheshire, UK SK10 4TJ; Study No. LR0589; 12/21/00); The skin of 5 Crl:CD rats/sex/group was exposed to 0 (deionized water), 2, 5, or 10 mg/kg/day of Dicrotophos technical (batch no. 403001B; purity: 87.6%) for 6 hours/day for 14 days. Upon the completion of this treatment regimen, the animals were maintained for another 2 weeks without treatment. Cholinesterase activity was assayed in the red blood cells and plasma of these animals on study days 2, 8, 15, 22 and 29. No deaths resulted from the treatment. No treatment-related clinical signs were evident. The mean body weights were not affected by the treatment. Red blood cell cholinesterase activity was 83 and 77% of the control group for the males in the 5 and 10 mg/kg treatment groups, respectively after 8 days of treatment ($p<0.01$). For the females, the maximal reduction in red blood cholinesterase was noted after 14 days of treatment for the 10 mg/kg treatment group (71% of control, $p<0.01$). For plasma cholinesterase activity, a maximal reduction for the males was evident after 14 days of treatment in the 5 and 10 mg/kg treatment groups (71 and 72% of control, respectively, $p<0.01$). A reduction in activity was still evident up to 7 days post-final treatment. For the females, maximal reduction in plasma cholinesterase activity was evident by study day 8 for the 5 and 10 mg/kg groups (64 and 55% of control, respectively, $p<0.01$) . The effect persisted through study day 15. **No adverse effect indicated. NOEL** was not established due to the limitation of the evaluated data. **Study supplemental** (non-guideline study). (Moore, 9/22/14)

299-017 036519 Brown, V. K. and L. W. Ferrigan, "Technical memorandum: Tox 16/65, Demyelination studies with the insecticide Bidrin," Tunstall Laboratory, July, 1965. In a study

which pre-dated current guidelines, and which had no QA oversight, Bidrin was administered to leghorn hens at 8 mg/kg to assess possible demyelination. The hens had been pre-treated with atropine and protopam chloride (pralidoxime chloride) to protect against acute toxicity. Eight of the 12 dosed hens survived, and were sacrificed after 3 weeks. Unspecified nerves were examined histologically, and no demyelination was evident. Since this report did not indicate adverse effects and could not be upgraded, no DPR worksheet is needed. Aldous, 12/1/14.

299-17 036520 Witherup, S., K. L. Stemmer, and H. Schlecht, "Specific physiological effects of Bidrin ®, Vapona ®, and Ciodrin ® insecticides in chickens," The Kettering Laboratory, Cincinnati, OH, Nov. 25, 1963. This is a brief report of a study evaluating possible delayed neuropathy due to 3 organophosphorus insecticides. The study design was free-form, and pre-dated current guidelines, hence is supplementary data. After a series of treatments to determine survivable dose levels, the definitive Bidrin delayed neuropathology study was conducted with 14 hens, each treated twice on day 1 with 1.5 mg/kg/dose, followed by a 1-week resting phase. Then in weeks 2 and 3, each hen received 0.75 mg/kg/day for 5 days each week. Clinical signs after the week 1 high dose exposures included weakness, unsteadiness, tremors, muscle fasciculations, diarrhea, salivation, lacrimation, and sometimes labored respiration and collapse. Following the lesser dosing during weeks 2-3, signs were limited to weakness and unsteadiness in several hens, with occasional observations of tremors and/or muscle fasciculations. At necropsy, at least some peripheral nervous and brain sections were examined for potential neuropathies. No neurohistopathology was associated with Bidrin or other insecticides evaluated, whereas positive controls (TOCP and trimethylphosphate) elicited varying degrees of peripheral demyelination and neurophagia in the brain cortex. Useful supplementary information. No DPR review is relevant. Aldous, Dec. 2, 2014.

Appendix II. DPR's SB950 Summary of Toxicology Data for Monocrotophos

CALIFORNIA DEPARTMENT OF FOOD AND AGRICULTURE
MEDICAL TOXICOLOGY BRANCH

SUMMARY OF TOXICOLOGY DATA

MONOCROTOPHOS (AZODRIN)

SB 950-095, Tolerance # 296

December 5, 1986
Revised April 2, 1987; January 8, 1988; Revised July 7, 1988

I. DATA GAP STATUS

Combined (chronic + onco) rat: No data gap, no adverse effect

Chronic dog: No data gap, no adverse effect

Onco mouse: No data gap, possible adverse effect (not onco)

Repro rat: No data gap, possible adverse effect

Terato rat: No data gap, no adverse effect

Terato rabbit: No data gap, no adverse effect

Gene mutation: No data gap, possible adverse effect

Chromosome: No data gap, possible adverse effect

DNA damage: No data gap, possible adverse effect

Neurotox: No data gap, no adverse effect

Note, Toxicology one-liners are attached
** indicates acceptable study;
Bold face indicates possible adverse effect.
Summary and previous revisions prepared by J.Gee; revised 1/8/88 by M.Harnois; revised July 7, 1988 by J. Gee.

II. TOXICOLOGY SUMMARY

COMBINED RAT

** 023 to 027 31654 to -59 "A Long-term Feeding Study with Azodrin in Rats to Investigate Chronic Toxicity and Oncogenicity (6, 12, 18 and 24 Month Necropsies.)" (Sittingbourne Research Centre, SBGR.82.062, 3/83) Monocrotophos (Batch no. 8-28-0-0, 78.7% E-isomer, 5.7% Z-isomer, possibly 12 other components), fed in the diet for 2 years to Wistar rats, 85/sex/test group and 170/sex in controls at 0, 0.01, 0.03, 0.1, 1.0 or 10.0 ppm (nominal). Initial review noted that the study was acceptable with remarkable findings as lipophage aggregates in the lung and a possible increase in pituitary tumors in females at 10 ppm (Gee, 11/12/85). A re-examination was made of the documents on file, especially those related to historical controls and dosage (033 48748-49). The re-examination found that previously noted effects were not biologically significant. Systemic NOEL (nom.) = 1.0 ppm (slight persistent decreased body weight in males); oncogenic NOEL (nom.) ≥10 ppm. Cholinesterase NOEL = 0.03 ppm. **No adverse effect; acceptable** . (Harnois, 1/6/88, Gee, 11/12/85 and 7/7/88)
EPA 1-liner: Supplementary. Systemic NOEL = 0.883 ppm, ChE NOEL = 0.026 ppm. Carcinogenic potential not determined pending the submission of historical control data. [See document 296-033, Record # 48749 for these data. EPA now grades the study as "minimum".]

033 48748 Supplement to 31654-59 consisting of EPA's comments and corrections prepared in 1984 and a 2-page Memorandum dated May 24, 1985, in which the conclusions on 6 studies are given. The 2-year rat study is "Minimum". Gee, 4/2/87.

033 48749 Supplement to 31654-59 consisting of historical control data from three experiments (no dates) for pituitary neoplasms. From the data given, with a high of 93.4% in decedent females, the biological significance of the incidence in the high dose females in the above study is in doubt, as discussed in the actual report. Gee, 4/2/87.

CHRONIC RAT

006 1145 Summary of 31654 - 59 reviewed under Rat, Combined, above. No data.

001 020972 (No lab, 1967) Summary of a study in rats, 25/sex/group, fed 0, 1, 10 or 100 ppm for 2 years. No data. Study said to be invalid and a replacement study initiated in 1978 (see above). J. Christopher, 5/24/85.

033 48750 Summary of 20972, study done at Woodard, 1967.

CHRONIC DOG

** 022 36153 "Azodrin Safety Evaluation by a Chronic Feeding Study in the Dog for Two Years - Final Report." (Woodard Res. Corp., 7/10/67) Monocrotophos (Code 7-3-4-16; 83% alpha isomer, 7% beta isomer, 4% DMMD); fed to 4/sex in controls, 3/sex at 0.16, 1.6 or 16 ppm for 2 years and 2/sex at 100 ppm, for 1 year; Cholinesterase NOEL = 1.6 ppm, nominal systemic NOEL = 16 ppm (salivation, soft stools and tremors); no histopathology findings reported. **No adverse effect reported**. Initially reviewed as unacceptable due to missing data (no individual clinical observations, stability problem in diet until storage conditions changed, no summary data, dose selection.) The study was upgraded to **acceptable** following the submission of supplemental data in Document 296-034, Record # 50450, consisting of individual data and summary tables. The study has some flaws by 1982 guidelines but contains sufficient data to determine that at the high doses, no chronic effect occurred other than cholinesterase inhibition. J. Gee, 11/8/85 and 4/2/87.
EPA 1-liner: Minimum. ChE NOEL = 1.6 ppm, systemic NOEL = 16 ppm (salivation and tremors).

034 50450 Supplement to 36153.

001 020973 Summary of 36153.

033 48750 Summary of 36153.

ONCOGENICITY, RAT

See under Combined Rat above.

ONCOGENICITY, MOUSE

**** 011 to 017 019973 to 019978** "Two Year Oncogenicity Study in Mice Fed Azodrin." (Shell Tox. Lab., London, 10/19/82). Monocrotophos (Batch 8-28-0-0; 78.7% E-isomer), fed in the diet at 0, 1, 2, 5 or 10 ppm to CD mice for 104 weeks, 77/sex/test group and 154/sex in control group. Initial review found 80% inhibition in plasma cholinesterase at high dose; plasma, brain and RBC cholinesterase depressed at all levels; dose-related increase in convulsions; cholinesterase NOEL < 1 ppm; no oncogenicity; acceptable with minor variations. (J. P. Christopher, 5/30/85). A review of additional

information (039 57703) confirmed the seizures as an adverse effect (increased numbers of animals affected; increased number of seizures/animal). Systemic NOEL <1 ppm for increased frequency of females with seizures; NOEL = 2 ppm for frequency of seizures in males; **acceptable**. (Harnois, 12/21/87 and Gee, 7/7/88)
EPA 1-liner (from 48748 in 033): Supplementary. Not oncogenic at 10 ppm (HDT). Strain of mouse not specified. [Shell has submitted additional data to EPA but the nature of these is not described.]

039 57703 Addendum to 011 019973 ff. EPA review comments and Registrant response. Identifies mice as Crl:CD (R)-1 (ICR)BR strain; cites references for spontaneous tumors. Respondent suggests that observations reported as convulsions were "fright induced seizures" rather than whole body contractions, gives frequency in controls of a comparable study as 18.3% for males and 3.0% for females and notes that the life-span of mice in 019973 was not decreased by the seizures. However, the dose-effect indicates that the frequency was related to the test substance. Respondent's comments indicate that retinopathy and lenticular degeneration were not related to treatment, but there are insufficient data in the report for an evaluation since most animals selected for this exam died before 2 years. (Harnois, 12/21/87)

REPRODUCTION, RAT

**** 028 36161 to -63** "A Reproduction Study in Rats Fed Azodrin." (Sittingbourne Res. Centre, SBGR.81.143, 11/81) Monocrotophos, Batch 8-28-0-0, 78.7% E-isomer, 5.7% Z-isomer, 0.2% trimethylphosphate plus 12 other components; fed in the diet to Wistar rats at 0, 0.1, 1, 3 or 10 ppm, 2 generations, 1 litter/generation; 13 males and 25-26 females per group; diets were prepared and analyzed weekly; used if ± 10% of nominal; loss of 6%/day in cage; food changed every 3-4 days; reproduction NOEL = 1 ppm (increased pre-weaning loss, "poor mammary development" in a few F0 and F1 dams at 10 ppm and f1 females at 3 ppm), systemic parental NOEL = 3 ppm nominal (lower body weight, smaller fecal pellets). Possible adverse effect on reproduction in the absence of significant parental toxicity. **Acceptable.** Gee, 11/13/85.
EPA 1-liner (from 48748 in 033): Minimum. NOEL (reproductive, parental, off-spring) = 2.7 ppm (decreased fertility, pup viability/weight, and lactation).

017 1147 Summary of 36161 - 63 above.

033 48751 Data Evaluation Record of EPA on 36161 - 63. Evaluated as core minimum with the following comments on deficiencies: Lack of food consumption (not required by 1982 USEPA Guidelines) precludes determination of intake, poor stability in diet meant actual concentration was an average of 13% lower than nominal, no data for the preliminary study upon which dose selection was based, no description of

how the 5 male and female pups were selected for histopathology, once daily observation was too infrequent allowing for cannibalization and/or autolysis and preventing determination of the length of gestation less than the nearest day (important in that this parameter appeared to be increased in time in the high dose), deficiency in vitamin K in the diet early in study and some statistical analyses and calculations were not performed. The conclusion, however, was that none of these was sufficient to cause the study to be rejected.

Pathology exam noted involuted mammary tissue apparently nonsecretory in the 3 high dose and one 3 ppm females whose litters apparently starved to death. Also, some liver changes were noted in weight and in histopathological exam.

EPA agrees that the body weight in the high dose males was affected by the test compound. Sufficiently high dose (10 ppm) was used with the signs of toxicity including increased incidence of abnormal fecal pellets at 10 and 3 ppm, body weight changes, pup mortality and reproductive effects. The reproductive effects were poorly developed teats, lactation problems, decreased viability and lactation indices.

Gee, 12/5/86.

001 020970 Summary of a 3-generation reproduction study in 10 males/20 females per group tested at 2, 5, 12 or 30 ppm in feed. No data but report states decreased litter weights at 12 and 30 ppm, stunting at 12 and 30, NOEL stated as 2 ppm. **Unacceptable**. J. Christopher, 5/24/85.
EPA 1-liner: Minimum. Reproduction NOEL = 2 ppm. Study identified as conducted at Hine, 3/66.

TERATOGENICITY, RAT

** 010 019972 "Technical AZODRIN (SD 9129) Teratology Study in SD CD Rats" (Toxigenics, Inc., 12/8/83) Monocrotophos (55F, 79% E isomer) was given by oral gavage at 0, 0.3, 1.0 or 2.0 mg/kg/day to mated female Sprague Dawley rats (26/ group) on days 6-15 of gestation. Maternal NOEL = 0.3 mg/kg/day (decrease in body weight); developmental NOEL = 1.0 ppm (decreased length and weight, increased unossified sternebrae). Initial review (J. P. Christopher, 5/28/85) found no adverse effect since no developmental effects noted in absence of maternal effect; report unacceptable but upgradeable with submission of analytical results on dosing solutions. Documents 033 48753 and 039 57702 contain data showing adequate concentration and stability under test conditions. (Harnois, 12/28/87) Upgraded to **acceptable** upon reconsideration that the technical material was adequately described - see 296-001. (Gee, 7/7/88)

033 48753 and 039 57702 Addenda to 010 19972. Analysis of material used in the study showed it to be 79% E isomer, but the composition of approx. 12% of the material remains unknown; analyses of the dosing

preparation showed nominal concentrations were closely approximated during the dosing period. (Harnois, 12/18/87)

033 48752 Review of rat teratology study (019972) by EPA. Conclusion is that monocrotophos is not teratogenic at the HDT and the study is CORE minimum. There is no discussion of study deficiencies. Gee, 12/5/86.

TERATOGENICITY, RABBIT

** 037 54478 "Developmental toxicity study of Azodrin Insecticide (Technical) in New Zealand White (NZW) Rabbits." (Argus Research, 1/12/87) Azodrin Technical (75%; Batch 13-4-0-0) in water was administered at 0, 0.1, 1, 3 or 6 mg/kg/day to artificially inseminated females on gestation days 6 through 18. 13 deaths in the 6 mg/kg/day group, and 1 death in the 3 mg/kg/day group. Maternal NOEL = 1 mg/kg/day (mortality, early delivery, clinical observations), dev. tox. NOEL = 3 mg/kg/day (increased resorptions) No adverse effects since no developmental toxicity without maternal toxicity; found unacceptable but upgradeable with submission of analyses of dosing solutions. (Gee, 4/2/87). Additional data were reviewed: historical information on lung agenesis (040 60522) indicated that frequencies observed in the 3 and 6 mg/kg/day groups were within the control range; information on purity and the results of dosing preparation analysis were submitted (039 57704), indicating that nominal concentrations were approximated during treatment. Unacceptable but upgradeable (composition of the test substance is needed). (Harnois, 12/18/87) Review of data in 296-001 indicates that the technical material used in the study had a composition close to the usual product. Study upgraded to **acceptable** status. (Gee, 7/7/88)

39 57704 Addendum to 037 54478. The test substance was identified as from batch 13-4-0-0, and stated to be 75% pure. No additional information on composition of this batch was given. The prepared dosing solutions contained the substance in essentially nominal amounts; the concentrations of stored samples were not appreciably changed during the period of dosing. (Harnois, 12/18/87)

40 60522 Historical control data for 037 54478. EPA reviewer noted frequency of agenesis of the diaphragmatic lobe of the lung to be increased at 3 and 6 mg/kg/day; data show the background frequency at the testing facility has increased and the frequencies at 3 and 6 mg/kg/day to be within control range; an Argus representative reported that the effect was due to genetic drift in the breeding stock (Hazleton/Dutchland). (Harnois, 12/18/87)

28 36160 "Toxicity Studies with Azodrin: Teratology Experiment in Rabbits Given Azodrin Orally." (Tunstall Lab, 10/72)

Monocrotophos technical, 40% w/v in hexylene glycol given in gelatin capsules at 0, 0.7 or 2 mg/kg, days 6 - 18; 32 in vehicle control, 16 in each test group with thalidomide as positive control; unclear whether the dose is based on the a.i. or technical grade Azodrin; maternal NOEL = 0.7 mg/kg (weight gain), developmental NOEL > 2 mg/kg. No adverse effect reported; **unacceptable** (no individual data, unclear dose levels; only 1/3 for visceral and 2/3 for skeletal - all fetuses should be examined for both; dose selection - report states 2 mg/kg the MTD based on a preliminary study but no data is presented - only marginal effect on body weight was noted in this study.) Gee, 11/13/85.
EPA 1-liner: Minimum. Teratogenic NOEL > 2 mg/kg/day; fetal toxicity NOEL > 2 mg/kg/day; maternal toxicity NOEL > 2 mg/kg/day.

001 952472 Summary of 36160.

MUTAGENICITY, GNMU

Microbial Systems

29 38547 "Toxicity Studies with Azodrin. Effect of Azodrin on Microorganisms in the Host-mediated Assay and in Vitro." (Turnstall Lab, 7/74) Serratia marcescens and Salmonella typhimurium strains TA1535, TA1536, TA1537 and TA1538, with technical grade Azodrin, 77.3%, by plate incorporation. Report states results were Negative. No data. **Unacceptable**. Gee, 11/8/85.

029 36164 "The Mutagenic Effect of Organophosphate Insecticides on Escherichia coli." (Tunstall Lab, 8/71) Monocrotophos as 24% solution, w/v, tested with Escherichia coli B/r WP2 strain in a screening of 9 pesticides; added on a filter disk, in triplicate. No adverse effect reported. **Unacceptable** (no data given). Gee, 11/8/85.

001 021435 Summary of a report on the Ames assay in Salmonella with no data. Unacceptable. Also included Escherichia coli with no data.

033 48755 "In vitro and In vivo Mutagenicity Studies of Environmental Chemicals." (SRI International, 1/84) Salmonella; monocrotophos, no purity stated; strains TA98, TA100 and TA1535, 1 plate per concentration, 3 trials at 0, 500, 1000, 2000, 3000, 4000 or 5000 ug/plate + S9 (trials 1 and 2) or 1000, 2500, 5000, 7500, 10,000 or 20,000 ug/plate + S9 (trial 3); concentration-dependent increase in revertants in TA100 + S9; **Unacceptable**, possibly upgradeable (no description of methods, 3 of 4 recommended strains, no description of test article, single plate per concentration.) Gee, 12/3/86.

033 48765 "In vitro and In vivo Studies of Selected Pesticides to Evaluate their Potential as Chemical Mutagens: In vitro Assays with Salmonella and E. coli." (SRI, Menlo Park, 11/13/75) Summary.

Salmonella strains TA1535, TA1537, TA1538, TA98 and TA100 + rat liver S9. Negative results stated. No data. Also, Escherichia coli WP2. Gee, 12/4/86.

Mammalian and Other Systems

033 48758 "In vitro and In vivo Mutagenicity Studies of Environmental Chemicals." (SRI International, 1/84) Mouse lymphoma L5178Y; monocrotophos, no purity stated; tested -S9, 0 to 900 ug/ml, 10 concentrations, +S9, 0 to 1200 ug/ml, 10 concentrations, based on toxicity, duplicate cultures; includes a preliminary study; increased mutant colonies with and without S9; **unacceptable** but upgradeable (no material and methods section, no description of test article.) Gee, 12/2/86.

036 51511 "Drosophila Mutagenesis Tests." (WARF, approximately 1976, R. Valencia) Twenty chemicals were tested for sex-linked recessive lethal effects at 0.1 to 4 ppm; CS/Y males crossed with FM6/FM6 females for P1 cross; no adverse effect reported; no data. **Unacceptable**. Gee, 4/1/87

SUMMARY: No one study as submitted is adequate to fill the data requirement but several could possibly be upgraded if missing information is submitted. Collectively, the reports provide sufficient evidence that monocrotophos is mutagenic both in bacteria and in mammalian cells and the data gap is considered filled with a possible adverse effect for genotoxicity. Gee, 4/2/87.

MUTAGENICITY, CHROMOSOME

029 36166 "Toxicity Studies on Azodrin: Dominant Lethal Assay in Male Mice after a Single Oral Dose of Azodrin." (Turnstall Lab, 9/73) Monocrotophos, >99%, Batch TSL/62/70/P; given in a single oral dose at 0, 1, 2 or 4 mg/kg to 12 males per group; mated 1:3 per week for 8 weeks; no toxic effects reported; NOEL > 4 mg/kg; **unacceptable** (no positive control; pregnancy rate of 60-80% resulted in fewer pregnant females than recommended; no justification of dose and no evidence MTD was approached; no individual data; not clear if given by gavage.) Gee, 11/12/85.
EPA 1-liner: Minimum. NOEL > 4 mg/kg (HDT).

036 51512 "Mammalian Screens." (SRI, no date) Ten pesticides were tested for dominant lethal effect in mice following feeding to males for 7 weeks. No adverse effects reported; no data for monocrotophos. **Unacceptable**. Gee, 4/1/87

001 1142 Summary of 36166.

033 48763 Summary of 36166.

033 48768 "In vitro and In vivo Studies of Selected Pesticides to Evaluate their Potential as Chemical Mutagens: Dominant Lethal Test with Azodrin in Mice." (SRI, Menlo Park, 11/13/75). Fed in the diet to ICR/SIM male mice for 8 weeks at 0, 15, 30 or 60 mg/kg; TEM as positive control; mated 1:2 for 7 days for 8 weekly periods. No data. Stated to be negative. Incomplete and **Unacceptable**. Summary only. Need full study. Gee, 12/4/86.

029 36167 "Toxicity Studies with Azodrin: Chromosome Studies on Bone Marrow Cells of Mice After a Single Oral Dose of Azodrin." (Turnstall Lab, 6/73). Monocrotophos, analytical grade, > 99%, Batch TSL/62/70/P, given in a single oral dose (by gavage?) to 8/sex/group at 0, 2 or 4 mg/kg to CF1 mice; sacrificed 4/sex/group at 8 and 24 hours after dosing; scored 100 cells per animal; no adverse effect on chromosomes or on animals is reported; NOEL > 4 mg/kg; **unacceptable** (inadequate high dose although selection was based on 1/4 and 1/2 the LD50, no positive control, no individual data, use of analytical rather than technical grade.) Gee, 11/12/85.
EPA 1-liner: No grade. NOEL > 4 mg/kg (HDT).

001, 6 and 17 021437 Summary of 36167.

033 48762 Summary of 36167.

033 48760 " In vitro and In vivo Mutagenicity Studies of Environmental Chemicals." (SRI International, 1/84) Micronucleus test; monocrotophos, no purity stated, given to 24/group (no sex or species indicated) at 0, 2, 4 or 8 mg/kg twice at 24-hour interval; sacrifice at 48, 72 and 96 hours; PCE/RBC ratios were not altered by treatment; no increase in micronuclei. TMP as positive control. **Unacceptable** (missing methods section, dose selection too low, no description of test article, no indication of number of cells scored.) Gee, 12/4/86.

036 51510 "Micronucleus Test on Monocrotophos." (SRI International, 1/10/80) Azodrin (lot no 9-SCL-77; no purity) given twice by i.p. injection at 0, 2, 4 or 8 mg/kg to 8 males (no females) per group per sacrifice time; sacrifices at 48, 72 or 96 hours after the first injection; 500 polychromatic erythrocytes scored per animal; some fluctuation in mean PCE/RBC with the mean for the high dose being slightly lower at all three sacrifice times; no mortality; **unacceptable** (no MTD used and use of males only without justification); no adverse effect reported. Report states that study meets all criteria "...except that of maximum tolerated dose." Further, the report states that the result should be confirmed by testing at a dose where some fatalities occur. This report contains the same data as in 48760. Gee, 4/1/87

033 48757 "In vitro and In vivo Mutagenicity Studies of

Environmental Chemicals." (SRI International, 1/84) In vitro sister chromatid exchange in CHO cells, monocrotophos, no purity stated, + S9 at 0, 0.0125, 0.025, 0.05, 0.1 or 0.2% for 2 hours with activation, at 0, 0.0025, 0.005, 0.01, 0.02 or 0.04% without activation. **Unacceptable** (missing material and methods section, no purity of test article), possibly upgradeable. Increase in sister chromatid exchanges with and without activation. Gee, 12/3/86.

SUMMARY: No one study as submitted is adequate to fulfill the data requirement but several might be upgraded if the complete reports were submitted. While the tests for gross chromosomal change (dominant lethal, micronucleus) appear to be negative, the positive SCE test indicated that changes within chromosomes may have been induced both with and without activation. The data gap is considered filled collectively by the studies submitted, with indications of a possible adverse genotoxic effect. Gee, 4/2/87.

MUTAGENICITY, DNA/OTHER

029 36165 "Toxicity Studies with Azodrin." Effect of Azodrin on Microorganisms in the Host-Mediated Assay and In Vitro. (Turnstall Lab, 7/74) JR(G), 11/12/85. Saccharomyces cerevisiae D4; monocrotophos technical, 77.3% w/v in hexylene glycol and analytical grade > 99%; CF1 male mice, 2/dose, were injected i.p. at 0, 4, 8, 12 mg/kg or at 2 and 4 mg/kg in repeat trial; yeast was injected i.p. immediately after dosing and the animals sacrificed at 5 hours; 4 plates each for tryptophan and for adenine revertants; for in vitro assay, both technical and analytical were used - technical at 0, 25, 39 or 50 mg/ml and analytical at 4, 5, 8, 10 or 50 mg/ml; adverse effect seen as increase in mitotic gene conversion loci in concentration-related manner; **unacceptable** (activation was not included in the in vitro assay for comparison, no individual plate counts.) Gee, 11/12/85.
EPA 1-liner: Minimum. Mutagen in Saccharomyces. Not a mutagen in Ser. marcescens or Sal. typhimurium. Weak mutagen detectable only at high conc. (5-50 mg/ml) in extremely sensitive system.

001 021436 Summary of 36165.

033 48764 Summary of 36165. Increase in gene conversion.

033 48761 Summary of host-mediated section of 36165. No adverse effect reported.

033 48766 "In vitro and In vivo Studies of Selected Pesticides to Evaluate their Potential as Chemical Mutagens: Mitotic Recombination in Saccharomyces." (SRI, Menlo Park, 11/13/75.) Saccharomyces D3

showed an increase in mitotic recombination without activation needed. No data. Escherichia coli P3478 and W3110 were negative for growth differential - no data. Bacillus subtilis M45 and H17, rec+/-, also were negative - no data. Gee, 12/4/86.

033 48756 "In vitro and In vivo Mutagenicity Studies of Environmental Chemicals." (SRI International, 1/84) Saccharomyces, monocrotophos, no purity stated; strain D3 (1 trial) and strain D7 (2 trials) + S9 at 0 to 5% w/v for D3 and 0 to 3% w/v for D7; adverse effect seen as a concentration-dependent increase in mitotic recombinants, gene conversion and reverse mutation; Salmonella rec+/- strains at 5 and 10 ul (concentration no given) showed differential growth in two trials; Salmonella uvrB +/- strains did not show differential growth. **Unacceptable** but possibly upgradeable with submission of the full report. No materials and methods are included, no purity of the test article. Gee, 12/3/86.

001 021595 Summary of a study using Saccharomyces cerevisiae. Tested at 8 and 50 mg/ml with no data. Summary states "Azodrin at high concentrations can produce lethal and mutagenic effects."

033 48759 "In vitro and In vivo Mutagenicity Studies of Environmental Chemicals." (SRI International, 1/84) Unscheduled DNA synthesis in WI-38 cells; monocrotophos, no purity stated; + S9 at 0, 1.2, 3.7, 11.1, 33.3 or 100 x 10^{-4} M, 6 replicates; 2 trials -S9, 1 trial +S9; positive effect with increase in DPM/ug DNA +S9; **Unacceptable** (missing materials and methods, no purity of test article), possibly upgradeable. Gee, 12/3/86.

033 48771 "Unscheduled DNA Synthesis Testing for Substitute Pesticides." A. Mitchell, SRI, author. Excerpt from "Substitute Chemical Program - The First Year of Progress. Proceedings from a Symposium, Vol. II. Toxicological Methods and Genetic Effects Workshop." Pages 151-153. Unscheduled DNA synthesis in WI-38 which were exposed for 3 hours -S9 and 1 hour +S9; measured incorporation of ^{3}H-thymidine in DNA by liquid scintillation. Azodrin positive + S9. **Unacceptable;** no data. May be same as 48759. Gee, 12/4/86.

033 48767 "In vitro and In vivo Studies of Selected Pesticides to Evaluate their Potential as Chemical Mutagens: Unscheduled DNA Synthesis Testing." (SRI, 11/13/75) Monocrotophos, no purity stated, with WI-38, incubated 3 hours -S9, 1 hour +S9, mouse liver to activate. Increase in incorporation of radioactive thymidine + S9. **Unacceptable,** no data. [Possibly same study as 48759.] Gee, 12/4/86.

SUMMARY: No one study as submitted is adequate to fill the data requirement
but several might be upgraded with the submission of the missing information. Collectively, the studies indicate positive genotoxic

effects in studies with several different endpoints, namely mitotic gene conversion and mitotic recombination in yeast and unscheduled DNA synthesis in mammalian cells. Gee, 4/2/87.

MISCELLANEOUS GENOTOXICITY STUDIES

001 021439 Summary of toxicity data indicating adverse genotoxic effects in a number of areas such as mitotic recombination, mutation, unscheduled DNA synthesis, sister chromatid exchange.

NEUROTOXICITY

029 36169 "Neurotoxicity Evaluation of Azodrin Insecticide: Subchronic Oral Administration in Hens." (Food and Drug Res. Lab., 6/22/81) Monocrotophos, 77.4%, given in gelatin capsules to 10 hens per group for 96 days at 0, 0.03, 0.1 or 0.3/0.5 mg/kg (dose raised on day 78); capsules were prepared daily; TOCP as positive control and an untreated as well as vehicle control group; plasma cholinesterase measured on days 1, 30, 58 and at sacrifice; histopathology on nerves of all animals; cholinesterase NOEL < 0.03%, NOEL (other) > 0.3%; **unacceptable** (not an acute delayed neurotoxicity study). Neurotoxic esterase inhibited in TOCP but not with monocrotophos. No adverse effect. Gee, 11/12/85.
EPA 1-liner: Minimum. Egg production NOEL = 0.1 mg/kg, neurological clinical score = 0, ChE plasma NOEL = 0.03 mg/kg.

001 952468 Summary of 36169.

008 1169 Rangefinding study for 36169. (Food and Drug Research Labs, 6/22/81) Monocrotophos given in gelatin capsules to 5 hens per group at 0, 0.03, 0.1, 0.3, or 1.0 mg/kg for 14 days. No data. **Unacceptable**. Christopher, 5/24/85.

028 36168 Rangefinding study for 36169 (same test as in 1169). Reviewed with 36169. 0.3 and 1 mg/kg inhibited brain cholinesterase; severe acute clinical signs in those given 1 mg/kg resulted in sacrifice of animals in this group.

033 48754 EPA evaluations of 1169 and 36169 neurotoxicity studies. Range-finding study called adequate as that type of study with egg production NOEL = 0.03 mg/kg, plasma cholinesterase NOEL = 0.03 mg/kg. For subchronic, 90-day study, the egg production NOEL = 0.1 mg/kg/day and no neurotoxicity was exhibited at 0.3 mg/kg b. wt. Grade CORE minimum. Gee, 9/2/86.

001 952466 Summary with no data. Hens (number not stated) were given a single oral dose of Azodrin at 6.7 mg/kg stated to be the LD50.

Dose was repeated at 21 days. Unacceptable.
EPA 1-liner: Supplementary. NOEL = 6.7 mg/kg (only level tested), Tunstall, 5/78.

Summary: In view of the negative findings in the 14-day (rangefinding) and 96-day studies, there is no deficiency in this area.

Appendix III. Dicrotophos BMD Analysis Summary

Appendix III - Dicrotophos BMD Analysis Summary

Acute ChE Study in Weanling Rats (Moxon 2003a)								
Model Name	**Test 1 p-value**	**Test 2 p-value**	**Test 3 p-value**	**Test 4 p-value**	**AIC**	**Scaled residual**	**BMD**	**BMDL**
Brain ChE PND8 Males								
Exponential2	< 0.0001	0.09192	0.4381	< 0.0001	-23.02857	-0.2574	0.0808944	0.0667684
Exponential3	< 0.0001	0.09192	0.4381	< 0.0001	-8.014203	-0.8502	0.393797	0.345824
Exponential4	< 0.0001	0.09192	0.4381	0.01601	-47.43038	0.09426	0.0723714	0.054721
Exponential5	< 0.0001	0.09192	0.4381	0.01601	-47.43038	0.09426	0.0723714	0.054721
Hill	<.0001	0.09192	0.4381	0.4027	-52.99864	0.498	0.052283	0.0342911
Notes: Non-homogeneous variance (Test 2 p < 0.1), but modeled variance good (Test 3 p > 0.1). Hill model has the best fit based on Test 4 (largest p-value), AIC (lowest value), scaled residuals (smallest value) and visual inspection.								
Brain ChE PND8 Females								
Exponential2	< 0.0001	0.005205	0.01575	< 0.0001	-13.17409	-0.4633	0.404161	0.361863
Exponential3	< 0.0001	0.005205	0.01575	< 0.0001	-3.820437	-6.07E-08	4.3534	0.0499999
Exponential4	< 0.0001	0.005205	0.01575	0.1177	-54.06762	1.366	0.0816853	0.0711499
Exponential5	< 0.0001	0.005205	0.01575	0.1177	-54.06762	1.366	0.0816853	0.0711499
Hill	<.0001	0.005205	0.01575	0.2002	-54.705386	0.982	0.0934706	0.0604787
Notes: Non-homogeneous variance (Test 2 p < 0.1), but modeled variance not good (Test 3 p < 0.1). However, model fit good (Test 4 p > 0.1) for Exp. 4 & 5 and Hill models and visually they look good. Selected Hill model based on highest Test 4 p-value, lowest AIC and scaled residuals.								
Brain ChE in PND15 Males								
Exponential2	< 0.0001	< 0.0001	0.01358	< 0.0001	0.6604104	0.04839	0.370011	0.335325
Exponential3	< 0.0001	< 0.0001	0.01358	< 0.0001	9.807209	1.49E-07	4.32585	0.29561
Exponential4	< 0.0001	< 0.0001	0.01358	0.4165	-36.12885	-0.7352	0.0787916	0.0696334
Exponential5	< 0.0001	< 0.0001	0.01358	0.4165	-36.12885	-0.7352	0.0787916	0.0696334
Hill	<.0001	<.0001	0.01358	0.315	-34.871277	-0.876	0.0701029	0.0378868
Notes: Non-homogenous variance (Test 2 < 0.1), variance not modeled well (Test 3 < 0.1). However, Model fit > 0.1 for Exp 4 & 5 and Hill. Visually they look good, too. Selected Exp. 4 & 5 since has lowest AIC values (same)								
Brain ChE PND15 Females								
Exponential2	< 0.0001	< 0.0001	0.01089	< 0.0001	2.118494	-0.1437	0.387246	0.346854
Exponential3	< 0.0001	< 0.0001	0.01089	< 0.0001	2.118494	-0.1437	0.387246	0.346854
Exponential4	< 0.0001	< 0.0001	0.01089	0.001306	-39.09553	-1.583	0.075378	0.0670426
Exponential5	< 0.0001	< 0.0001	0.01089	0.001306	-39.09553	-1.583	0.075378	0.0670426
Hill	<.0001	<.0001	0.01089	0.05379	-46.532536	0.73	0.0344049	0.028421
Notes: Non-homogenous variance (Test 2 p < 0.1), variance not modeled well (Test 3 p < 0.1). Test 4 (model fit) p < 0.1 for all, so no model selected.								

Appendix III - Dicrotophos BMD Analysis Summary

Acute ChE Study in Weanling Rats (Moxon 2003a) - continued								
Model Name	**Test 1 p-value**	**Test 2 p-value**	**Test 3 p-value**	**Test 4 p-value**	**AIC**	**Scaled residual**	**BMD**	**BMDL**
Brain ChE PND22 Males								
Exponential2	< 0.0001	0.001478	0.03803	< 0.0001	9.973987	0.5647	0.372171	0.0900431
Exponential3	< 0.0001	0.001478	0.03803	< 0.0001	9.973987	0.5647	0.372171	0.0900431
Exponential4	< 0.0001	0.001478	0.03803	0.07834	-19.04476	-0.3757	0.108486	0.0924896
Exponential5	< 0.0001	0.001478	0.03803	0.5022	-21.68767	0.1891	0.228194	0.130349
Hill	<.0001	0.001478	0.03803	0.3899	-21.39892	0.166	0.246701	0.155007
Notes: Non-homogeneous variance (Test 2 p < 0.1), variance not modeled well (Test 3 p < 0.1), but model fit good (Test 4 p > 0.1) for Exp. 5 and Hill models. Exp. 5 selected because it had highest Test 4 p-value, lowest AIC. although scaled residuals smaller for Exp. 4 and Hill.								
Brain ChE PND22 Females								
Exponential2	< 0.0001	0.4458	0.4458	< 0.0001	6.184603	-0.69	0.239391	0.145676
Exponential3	< 0.0001	0.4458	0.4458	< 0.0001	6.184603	-0.69	0.239391	0.145676
Exponential4	< 0.0001	0.4458	0.4458	0.01321	-20.70647	-2.131	0.11501	0.0940254
Exponential5	< 0.0001	0.4458	0.4458	0.01321	-20.70647	-2.131	0.11501	0.0940254
Hill	<.0001	0.4458	0.4458	0.03954	-22.899641	-1.85	0.0825515	0.0635846
Notes: Constant varinace (Test 2 p > 0.1), but model fit poor for all (Test 4 p < 0.1), so no model selected.								

Acute ChE Study in PND42 Rats (Brammer 2002a)								
Model Name	**Test 1 p-value**	**Test 2 p-value**	**Test 3 p-value**	**Test 4 p-value**	**AIC**	**Scaled residual**	**BMD**	**BMDL**
Brain ChE Males - Day 1								
Exponential2	< 0.0001	0.003264	0.109	0.3533	-23.62381	0.0594	0.380441	0.362614
Exponential3	< 0.0001	0.003264	0.109	0.2448	-22.35187	-0.5367	0.643489	0.365455
Exponential4	< 0.0001	0.003264	0.109	0.3533	-23.62381	0.0594	0.380441	0.219588
Exponential5	< 0.0001	0.003264	0.109	N/A	-20.90139	-0.2182	0.314321	0.261081
Hill	<.0001	0.003264	0.109	N/A	-20.901385	-0.218	0.316638	
Notes: Non-homogeneous variance (Test 2 p < 0.1), but variance modeled well (Test 3 p > 0.1). Exp. 2 & 4 have the best fit with identical Test 4 p-values, AICs and scaled residuals, but Exp. 4 has lower BMDL, so selected as a precaution. U.S. EPA selected same model BMD and BMDL estimates.								
Brain ChE Females - Day 1								
Exponential2	< 0.0001	< 0.0001	0.06722	0.003977	-23.6416	-1.974	0.391518	0.375628
Exponential3	< 0.0001	< 0.0001	0.06722	0.003977	-23.6416	-1.974	0.391518	0.375628
Exponential4	< 0.0001	< 0.0001	0.06722	0.6747	-32.52009	-0.1584	0.120262	0.0920115
Exponential5	< 0.0001	< 0.0001	0.06722	0.6747	-32.52009	-0.1584	0.120262	0.0920115
Hill	<.0001	<.0001	0.06722	N/A	-12.818981	-2.3	1.44747	0.0408037
Notes: Non-homogeneous variance (Test 2 p < 0.1), variance not modeled well (Test 3 p < 0.1). However, Exp. 4 & 5 have Test 4 p-values > 0.1 which are identical along with identical AICs, scaled residuals, BMD and BMDLs. So BMD and BMDL estimate from these two models selected.								

Appendix III - Dicrotophos BMD Analysis Summary

Acute Neurotoxicity Study in Rats (Rattray 1995)								
Model Name	**Test 1 p-value**	**Test 2 p-value**	**Test 3 p-value**	**Test 4 p-value**	**AIC**	**Scaled residual**	**BMD**	**BMDL**
Brain ChE Males - Day 1								
Exponential2	< 0.0001	0.04163	0.8862	< 0.0001	12.0494	-1.468	0.340923	0.277044
Exponential3	< 0.0001	0.04163	0.8862	< 0.0001	12.0494	-1.468	0.340922	0.277044
Exponential4	< 0.0001	0.04163	0.8862	0.3054	-4.46674	-0.7558	0.251533	0.212999
Exponential5	< 0.0001	0.04163	0.8862	0.3054	-4.46674	-0.7558	0.251533	0.212999
Hill	<.0001	0.04163	0.8862	N/A	-3.517124	0.0146	0.231767	0.151214
Notes: Non-homogeneous variance (Test 2 p < 0.1), but variance modeled well (Test 3 p > 0.1). Exp. 4 & 5 have Test 4 p-values > 0.1 which were identical along with same AICs, scaled residuals, BMD and BMDLs. So the BMD and BMDL from these models selected.								
Brain ChE Females - Day 1								
Exponential2	< 0.0001	0.5636	0.5636	0.0002391	0.0169947	-1.736	0.328829	0.289791
Exponential3	< 0.0001	0.5636	0.5636	0.0002391	0.0169947	-1.736	0.328829	0.289791
Exponential4	< 0.0001	0.5636	0.5636	0.1383	-12.46306	0.5891	0.244478	0.209277
Exponential5	< 0.0001	0.5636	0.5636	0.1383	-12.46306	0.5891	0.244478	0.209277
Hill	<.0001	0.5636	0.5636	N/A	-12.660222	5.09E-07	0.239289	0.185115
Notes: Constant variance (Test 2 p > 0.1), so variance not modeled (Note: Test 2 & 3 have same p-values). Test 4 p-value could not be calculated for Hill model, but it has lowest AIC and scaled residuals, so it was selected.								

7-Day ChE Study in Weanling Rats (Moxon 2003b)								
Model Name	**Test 1 p-value**	**Test 2 p-value**	**Test 3 p-value**	**Test 4 p-value**	**AIC**	**Scaled residual**	**BMD**	**BMDL**
Brain ChE PND18 Males								
Exponential2	< 0.0001	0.001009	0.3853	0.1075	13.18283	0.01437	0.0639084	0.0553471
Exponential3	< 0.0001	0.001009	0.3853	0.03187	15.98787	3.33E-07	0.359494	0.0542734
Exponential4	< 0.0001	0.001009	0.3853	0.1075	13.18283	0.01437	0.0639084	0.0315121
Exponential5	< 0.0001	0.001009	0.3853	0.051	15.04774	-0.227	0.0868814	0.032075
Hill	<.0001	0.001009	0.3853	0.0152	16.989238	-0.21	0.0814847	0.0305023
Notes: Non-homogeneous variance (Test 2 p < 0.1), but variance modeled well (Test 3 p > 0.1). Exp. 2 & 4 had highest Test 4 p-values and the same AIC and scaled residuals, but Exp. 4 had lower BMDL so the estimates from this model selected. U.S. EPA selected the same model BMD and BMDL								
Brain ChE PND18 Females								
Exponential2	< 0.0001	0.00217	0.05594	0.4102	-6.610589	0.5855	0.0494189	0.0444033
Exponential3	< 0.0001	0.00217	0.05594	< 0.0001	722.4313	0	0.0496049	0.00166138
Exponential4	< 0.0001	0.00217	0.05594	0.4102	-6.610589	0.5855	0.0494189	0.0284767
Exponential5	< 0.0001	0.00217	0.05594	0.1701	-3.611014	0.2945	0.0775558	0.0317548
Hill	<.0001	0.00217	0.05594	0.1701	-3.611014	0.295	0.0773429	0.0308368
Notes: Non-homogeneous variance (Test 2 p < 0.1), but variance not modeled well (Test 3 < 0.1). Test 4 p-values (> 0.1) highest for Exp. 2 & 4 with identical AICs and scaled residuals, but Exp. 4 had lower BMDL, so this model BMD and BMDL selected. U.S. EPA selected the same model BMD and								

Appendix III - Dicrotophos BMD Analysis Summary

7-Day ChE Study in Weanling Rats (Moxon 2003b) - continued								
Model Name	**Test 1 p-value**	**Test 2 p-value**	**Test 3 p-value**	**Test 4 p-value**	**AIC**	**Scaled residual**	**BMD**	**BMDL**
Brain ChE PND48 Males								
Exponential2	< 0.0001	0.002484	0.00214	0.2823	0.8896673	0.5711	0.107237	0.087504
Exponential3	< 0.0001	0.002484	0.00214	0.2183	2.119894	-0.0187	0.177869	0.0903093
Exponential4	< 0.0001	0.002484	0.00214	0.2823	0.8896673	0.5711	0.107237	0.0538057
Exponential5	< 0.0001	0.002484	0.00214	0.09104	3.932167	0.1969	0.086822	0.0634267
Hill	<.0001	0.002484	0.00214	0.09104	3.932167	0.197	0.0872937	0.0631821
Notes: Non-homogeneous variance (Test 2 p < 0.1), but variance not modeled well (Test 3 p < 0.1). Exp. Test 4 p-values (> 0.1) highest for Exp 2 & 4 with identical AIC and scaled residuals, but BMDL lower with Exp. 4 so this BMD and BMDL for selected. U.S. EPA selected same BMD and BMDL.								
Brain ChE PND48 Females								
Exponential2	< 0.0001	0.2672	0.2672	0.0019	1.753604	0.945	0.0903817	0.0690732
Exponential3	< 0.0001	0.2672	0.2672	0.002408	0.9066065	-0.1895	0.202611	0.0886113
Exponential4	< 0.0001	0.2672	0.2672	0.0019	1.753604	0.945	0.0903817	0.058109
Exponential5	< 0.0001	0.2672	0.2672	0.0005462	2.799951	4.65E-08	0.0900642	0.0773327
Hill	<.0001	0.2672	0.2672	0.0005462	2.799951	1.38E-05	0.0904683	0.077037
Notes: Constant variance (Test 2 p > 0.1), but Test 4 failed for all models so no model selected.								

28-Day ChE Study in Rats (Brammer 2002c)								
Model Name	**Test 1 p-value**	**Test 2 p-value**	**Test 3 p-value**	**Test 4 p-value**	**AIC**	**Scaled residual**	**BMD**	**BMDL**
Brain ChE Males - Day 29								
Exponential2	< 0.0001	0.003831	0.0176	0.6211	10.0534	0.1746	0.0603784	0.0511959
Exponential3	< 0.0001	0.003831	0.0176	0.523	11.50862	-1.04E-08	0.358392	0.0521715
Exponential4	< 0.0001	0.003831	0.0176	0.6211	10.0534	0.1746	0.0603784	0.0152893
Exponential5	< 0.0001	0.003831	0.0176	N/A	13.50862	-2.18E-08	0.262378	0.0175685
Hill	<.0001	0.003831	0.0176	N/A	13.508624	2.70E-07	0.245099	0.0173622
Notes: Non-homogeneous variance (Test 2 p < 0.1), but variance not modeled well (Test 3 p < 0.1). Exp. Test 4 p-values (> 0.1) highest for Exp 2 & 4 with identical AIC and scaled residuals, but BMDL lower with Exp. 4 so this BMD and BMDL for selected. U.S. EPA selected same BMD and BMDL.								
Brain ChE Females - Day 29								
Exponential2	< 0.0001	0.08335	0.06877	0.2484	7.58674	-0.7313	0.0768945	0.0587043
Exponential3	< 0.0001	0.08335	0.06877	0.2484	7.58674	-0.7313	0.0768945	0.0587043
Exponential4	< 0.0001	0.08335	0.06877	0.5246	7.206435	-0.4916	0.0124188	0.0058289
Exponential5	< 0.0001	0.08335	0.06877	0.5246	7.206435	-0.4916	0.0124188	0.0058289
Hill	<.0001	0.08335	0.06877	0.5807	7.106696	-0.421	0.0112456	0.00432925
Notes: Non-homogeneous variance (Test 2 p < 0.1), but variance not modeled well (Test 3 p < 0.1). All models had Test 4 p-values > 0.1. Hill model had highest Test 4 p-value, lowest AIC, smallest scaled residuals, so selected this model.								

Appendix III - Dicrotophos BMD Analysis Summary

Subchronic Neurotoxicity Study in Rats (Horner 1995)								
Model Name	**Test 1 p-value**	**Test 2 p-value**	**Test 3 p-value**	**Test 4 p-value**	**AIC**	**Scaled residual**	**BMD**	**BMDL**
Brain ChE Males - Week 5								
Exponential2	< 0.0001	< 0.0001	0.7519	< 0.0001	27.73567	1.439	0.108123	0.101367
Exponential3	< 0.0001	< 0.0001	0.7519	< 0.0001	27.73567	1.439	0.108123	0.101367
Exponential4	< 0.0001	< 0.0001	0.7519	0.8752	-17.59285	-0.06216	0.0386449	0.0360282
Exponential5	< 0.0001	< 0.0001	0.7519	0.8752	-17.59285	-0.06216	0.0386449	0.0360282
Hill	<.0001	<.0001	0.7519	N/A	-15.61753	0.054	0.0367463	0.022866
Notes: Non-homogeneous variance (Test 2 p < 0.1), but variance modeled well (Test 3 p > 0.1). Exp. 4 & 5 have highest Test 4 p-values with same AICs and scaled residuals, BMDs and BMDLs. So the BMD and BMDL estimates from these two models selected.								
Brain ChE Females - Week 5								
Exponential2	< 0.0001	0.03006	0.8159	< 0.0001	23.97809	-0.7961	0.0528987	0.044071
Exponential3	< 0.0001	0.03006	0.8159	< 0.0001	34.2407	0.5835	0.115904	0.0340592
Exponential4	< 0.0001	0.03006	0.8159	0.3608	6.854796	-0.6491	0.0477914	0.0418788
Exponential5	< 0.0001	0.03006	0.8159	0.3608	6.854796	-0.6491	0.0477914	0.0418788
Hill	<.0001	0.03006	0.8159	0.8655	6.048278	-0.103	0.0323717	0.0258915
Notes: Non-homogeneous variance (Test 2 p < 0.1), but variance modeled well (Test 3 > 0.1). Hill model has highest Test 4 p-value (> 0.1) and lowest AIC and scaled residuals. So BMD and BMDL estimates from this model selected.								
Brain ChE Males - Week 9								
Exponential2	< 0.0001	0.0878	0.3173	< 0.0001	20.43647	-2.19	0.0459923	0.0391321
Exponential3	< 0.0001	0.0878	0.3173	< 0.0001	4522.071	2.53E+107	0.104269	Bad_Completion
Exponential4	< 0.0001	0.0878	0.3173	0.002879	3.769272	-2.023	0.0424146	0.0377703
Exponential5	< 0.0001	0.0878	0.3173	0.002879	3.769272	-2.023	0.0424146	0.0377703
Hill	<.0001	0.0878	0.3173	0.03516	-0.675649	-1.56	0.0282579	0.0234663
Notes: Non-homogeneous variance (Test 2 p < 0.1), but variance modeled well (Test 3 > 0.1), but model fit poor for all models so no model selected.								
Brain ChE Females - Week 9								
Exponential2	< 0.0001	< 0.0001	0.3518	< 0.0001	29.18429	1.129	0.119816	0.111804
Exponential3	< 0.0001	< 0.0001	0.3518	< 0.0001	22826.44	0	0.115321	Bad_Completion
Exponential4	< 0.0001	< 0.0001	0.3518	0.257	-11.00568	-0.7133	0.0443778	0.0409235
Exponential5	< 0.0001	< 0.0001	0.3518	0.257	-11.00568	-0.7133	0.0443778	0.0409236
Hill	<.0001	<.0001	0.3518	0.9079	-12.277142	0.0207	0.0286734	0.0249339
Notes: Non-homogeneous variance (Test 2 p < 0.1), but variance modeled well (Test 3 > 0.1). Hill model has highest Test 4 p-value (> 0.1) and lowest AIC and scaled residuals. So BMD and BMDL estimates from this model selected.								

Appendix III - Dicrotophos BMD Analysis Summary

Subchronic Neurotoxicity Study in Rats (Horner 1995) - continued								
Model Name	**Test 1 p-value**	**Test 2 p-value**	**Test 3 p-value**	**Test 4 p-value**	**AIC**	**Scaled residual**	**BMD**	**BMDL**
Brain ChE Males - Week 14								
Exponential2	< 0.0001	0.007105	0.08708	< 0.0001	3.226581	-1.434	0.0507201	0.045494
Exponential3	< 0.0001	0.007105	0.08708	< 0.0001	17.26518	1.22	0.114823	0.107812
Exponential4	< 0.0001	0.007105	0.08708	0.1392	-20.61266	-0.953	0.0475727	0.0440646
Exponential5	< 0.0001	0.007105	0.08708	0.1392	-20.61266	-0.953	0.0475727	0.0440646
Hill	<.0001	0.007105	0.08708	0.5912	-22.511065	-0.345	0.0344751	0.0306639
Notes: Non-homogeneous variance (Test 2 p < 0.1), but variance not modeled well (Test 3 < 0.1). Test 4 p > 0.1 for several models. Hill model selected because it had highest Test 4 p-value and lowest AIC and scaled residuals.								
Brain ChE Females - Week 14								
Exponential2	< 0.0001	0.0001889	0.8098	< 0.0001	29.02647	1.096	0.130213	0.121365
Exponential3	< 0.0001	0.0001889	0.8098	< 0.0001	29.02647	1.096	0.130213	0.121365
Exponential4	< 0.0001	0.0001889	0.8098	0.1375	-13.6472	-1.02	0.0451815	0.0417724
Exponential5	< 0.0001	0.0001889	0.8098	0.1375	-13.6472	-1.02	0.0451815	0.0417724
Hill	<.0001	0.0001889	0.8098	0.6915	-15.695707	-0.27	0.0290696	0.0254562
Notes: Non-homogeneous variance (Test 2 < 0.1), but variance modeled well (test 3 p > 0.1). Test 4 p > 0.1 for several models. Hill model was selected based on having the highest Test 4 p and lowest AIC, even though Exp. 4 & 5 has smallest scaled residuals.								

28-Day Inhalation Study in Rats (Blair 2010)								
Model Name	**Test 1 p-value**	**Test 2 p-value**	**Test 3 p-value**	**Test 4 p-value**	**AIC**	**Scaled residual**	**BMD**	**BMDL**
Brain ChE Males								
Exponential2	< 0.0001	0.04441	0.09846	0.5909	295.0835	-0.7012	0.704795	0.652324
Exponential3	< 0.0001	0.04441	0.09846	< 0.0001	722.8498	0.0007842	1.06425	Bad_Completion
Exponential4	< 0.0001	0.04441	0.09846	0.617	296.2814	0.04856	0.584922	0.428418
Exponential5	< 0.0001	0.04441	0.09846	N/A	298.0312	0.1054	0.649747	0.434643
Hill	<.0001	0.04441	0.09846	NA	298.065475	0.105	0.703526	0.573142
highest Test 4 p-value even though Exp. 2 model has lowest AIC. Exp. 4 also more similar to results from Exp. 5 and results from Exp. 4 & 5 and Hill for females.								

Appendix III - Dicrotophos BMD Analysis Summary

28-Day Inhalation Study in Rats (Blair 2010) - continued								
Model Name	**Test 1 p-value**	**Test 2 p-value**	**Test 3 p-value**	**Test 4 p-value**	**AIC**	**Scaled residual**	**BMD**	**BMDL**
Brain ChE Females								
Exponential2	< 0.0001	0.05727	0.0527	0.08459	304.3568	-0.8776	0.673254	0.606137
Exponential3	< 0.0001	0.05727	0.0527	< 0.0001	1368.439	367700	0.672528	0.00931213
Exponential4	< 0.0001	0.05727	0.0527	0.08474	304.3885	0.3025	0.487733	0.352589
Exponential5	< 0.0001	0.05727	0.0527	0.08474	304.3885	0.3025	0.487732	0.352589
Hill	<.0001	0.05727	0.0527	0.08893	304.310709	0.347	0.476344	0.408322
Notes: Non-homogeneous variance (Test 2 p < 0.1), but variance not modeled well (Test 3 p < 0.1). Test 4 p-values < 0.1 for all models, but considered acceptable because close to 0.1. Selected Hill model based on highest Test 4 p-value and lowest AIC, even though scaled residuals lower for Exp. 4 & 5.								

28-Day Dermal Study in Rats (Noakes 2001)								
Model Name	**Test 1 p-value**	**Test 2 p-value**	**Test 3 p-value**	**Test 4 p-value**	**AIC**	**Scaled residual**	**BMD**	**BMDL**
Brain ChE Males								
Exponential2	< 0.0001	0.737	0.737	0.01057	2.434781	-2.404	9.94238	7.45725
Exponential3	< 0.0001	0.737	0.737	0.01057	2.434781	-2.404	9.9424	7.45725
Exponential4	< 0.0001	0.737	0.737	0.0615	-1.21198	1.817	3.6661	2.41499
Exponential5	< 0.0001	0.737	0.737	0.09162	-1.943926	-8.74E-05	8.52006	3.50191
Hill	<.0001	0.737	0.737	0.09161	-1.943766	-6.82E-05	8.38103	3.84651
Notes: Constant variance (Test 2 > 0.1). Test 4 p < 0.1 for all models, but close to 0.1 for Exp. 5 and Hill. Selected Exp. 5 based on highest Test 4 p-value, and lowest AIC and scaled residual. U.S. EPA selected Exp. 4 model based on better visual fit even though AIC lower for Exp. 5 and Test 4 p-value is								
Brain ChE Females								
Exponential2	< 0.0001	< 0.0001	0.02657	0.06649	3.059048	-1.117	8.70721	7.86559
Exponential3	< 0.0001	< 0.0001	0.02657	< 0.0001	1304.242	0	8.62764	Bad_Completion
Exponential4	< 0.0001	< 0.0001	0.02657	0.1729	1.393194	-1.046	3.348	2.13974
Exponential5	< 0.0001	< 0.0001	0.02657	0.1729	1.393194	-1.046	3.348	2.13974
Hill	<.0001	<.0001	0.02657	0.1682	1.448129	-1.01	3.09263	1.72982
Notes: Non-homogeneous variance (Test 2 p <0.1), variance not modeled well (Test 3 P < 0.1), but Test 4 p > 0.1 for several models. Exp. 4 & 5 were selected since they had the highest Test 4 p-values with same AICs, scaled residuals, BMDs and BMDLs.								

Appendix III - Dicrotophos BMD Analysis Summary

2-Yr Chronic Toxicity Study in Rats (Allen 1998)								
Model Name	**Test 1 p-value**	**Test 2 p-value**	**Test 3 p-value**	**Test 4 p-value**	**AIC**	**Scaled residual**	**BMD**	**BMDL**
Brain ChE Wk53 Males								
Exponential2	< 0.0001	0.005634	0.002084	< 0.0001	21.10312	-2.639	0.0300134	0.0259369
Exponential3	< 0.0001	0.005634	0.002084	< 0.0001	21.10312	-2.639	0.0300134	0.0259369
Exponential4	< 0.0001	0.005634	0.002084	< 0.0001	4.407792	-2.45	0.0276746	0.0247364
Exponential5	< 0.0001	0.005634	0.002084	< 0.0001	4.407792	-2.45	0.0276746	0.0247364
Hill	<.0001	0.005634	0.002084	0.0001958	-2.343159	-2.26	0.0175508	0.0140835
Notes: Non-homogenous variance (Test 2 < 0.1), variance not modeled well (Test 3 p < 0.1) and model fit poor (Test 4 p < 0.1) for all models.								
Brain ChE Wk53 Females								
Exponential2	< 0.0001	< 0.0001	0.000457	0.004695	59.71509	-0.2597	0.0956609	0.084013
Exponential3	< 0.0001	< 0.0001	0.000457	< 0.0001	2205.195	0	0.0955059	Bad_Completion
Exponential4	< 0.0001	< 0.0001	0.000457	0.07738	54.11166	-1.168	0.0473812	0.0369167
Exponential5	< 0.0001	< 0.0001	0.000457	0.07738	54.11166	-1.168	0.0473812	0.0369167
Hill	<.0001	<.0001	0.000457	0.1094	53.555156	-1.11	0.036684	0.0249788
Notes: Non-homogenous variance (Test 2 p < 0.1), variance not modeled well (Test 3 p < 0.1). Test 4 p-value > 0.1 only for Hill model which also had lowest AIC and scaled residuals. So Hill model selected.								
Brain ChE Wk100 Males								
Exponential2	< 0.0001	0.573	0.573	0.1273	2.582342	-1.158	0.0266922	0.0224428
Exponential3	< 0.0001	0.573	0.573	0.1273	2.582342	-1.158	0.0266922	0.0224428
Exponential4	< 0.0001	0.573	0.573	N/A	2.256713	1.84E-07	0.0160799	0.0109029
Exponential5	< 0.0001	0.5651	0.5651	0.1603	1.283947	-1.065	0.0244208	0.0199295
Notes: Constant variance (Test 2 p > 0.1). Exp. 5 model selected because it had highest Test 4 p-value and lowest AIC and scaled residuals.								
Brain ChE Wk105 Females								
Exponential2	< 0.0001	0.0003184	0.0003727	0.002984	30.36762	-1.49	0.0424529	0.0340801
Exponential3	< 0.0001	0.0003184	0.0003727	< 0.0001	3466.955	0	0.0815883	Bad_Completion
Exponential4	< 0.0001	0.0003184	0.0003727	0.08976	23.61754	-1.074	0.042056	0.0345724
Exponential5	< 0.0001	0.0003184	0.0003727	0.08976	23.61754	-1.074	0.042056	0.0345724
Hill	<.0001	0.0003184	0.0003727	0.1553	22.758024	-0.939	0.0315186	0.0230422
Notes: Non-homogenous variance (Test 2 p < 0.1), but variance not modeled well (Test 3 p < 0.1). Selected Hill model since was only model with Test 4 p-value > 0.1 and it had th elowest AIC, even though other models had lower scaled residuals.								

Appendix III - Dicrotophos BMD Analysis Summary

1-Yr Chronic Toxicity Study in Dogs (Horner 1997)								
Model Name	**Test 1 p-value**	**Test 2 p-value**	**Test 3 p-value**	**Test 4 p-value**	**AIC**	**Scaled residual**	**BMD**	**BMDL**
Brain ChE Males - Wk 53								
Exponential2	0.0001555	0.247	0.247	0.9467	9.416569	0.2776	0.0691343	0.0516554
Exponential3	0.0001555	0.247	0.247	0.9297	11.31477	0.03015	0.086578	0.0519522
Exponential4	0.0001555	0.247	0.247	0.9467	9.416569	0.2776	0.0691343	0.0339247
Exponential5	0.0001555	0.247	0.247	N/A	13.31477	0.03015	0.0865781	0.0519522
Hill	0.0001555	0.247	0.247	0.9726	11.308175	0.00836	0.0854839	0.0320414
Notes: Constant variance (Test 2 p > 0.1). Exp. 2 & 4 had highest Test 4 p-values with same AIC and scaled residual. Exp. 4 model was selected because it had lower BMDL. U.S. EPA did not perform BMD analysis of this data.								
Brain ChE in Females - Wk 53								
Exponential2	0.0005398	0.1304	0.1304	0.4858	9.542987	-0.9366	0.100271	0.0719357
Exponential3	0.0005398	0.1304	0.1304	0.4858	9.542987	-0.9366	0.100271	0.0719357
Exponential4	0.0005398	0.1304	0.1304	0.9538	10.10262	-0.04613	0.0469945	0.0222503
Exponential5	0.0005398	0.1304	0.1304	0.9538	10.10262	-0.04613	0.0469945	0.0222503
Hill	0.0005398	0.1304	0.1304	NA	12.099263	3.82E-07	0.0445458	0.0168109
Notes: Constant variance. Test 4 p-values suggest Exp. $ & 5 have best fit, but Exp. 2 & 3 have lowest AIC and smallest scaled residuals. BMD and BMDL same for both..								

Appendix IV. DEEM-FCID Summary Reports for Dicrotophos Dietary and Drinking Water Exposure Assessments

Ver. 4.02, 05-10-c
DEEM-FCID Acute analysis for DICROTOPHOS
Residue file name: H:\MyFiles\DEEM-FCID Files\Dicrotophos\Dicrotophos v4.02 Files\dicrotophos acute food ppb.R10
Analysis Date 12-14-2016 Residue file dated: 12-14-2016/08:53:14
Reference dose: aRfD = 0.3 mg/kg bw/day NOEL = 30 mg/kg bw/day
Comment: Dose in ug/kg/day, Residue in ppb

EPA Code	Crop Grp	Food Name	Def Res (ppm)	Adj.Factors #1	#2	Comment
2003128000	20C	Cottonseed, oil	40.000000	1.000	1.000	residu
		Full comment: residue in ppb				
2003128001	20C	Cottonseed, oil-babyfood	40.000000	1.000	1.000	

Ver. 4.02, 05-10-c
DEEM-FCID ACUTE Analysis for DICROTOPHOS NHANES 2005-2010 2-Day
Residue file: dicrotophos acute food ppb.R10 Adjustment factor #2 NOT used.
Analysis Date: 12-14-2016/08:55:53 Residue file dated: 12-14-2016/08:53:14
NOEL (Acute) = 30.000000 mg/kg body-wt/day
RAC/FF intake summed over 24 hours
Run Comment: "Dose in ug/kg/day, Residue in ppb"
==========

Summary calculations--per capita:

--- 95th Percentile----			--- 97.5th Percentile----			---99.9th Percentile----		
Exposure	% aRfD	MOE	Exposure	% aRfD	MOE	Exposure	% aRfD	MOE
Total US Population:								
0.003139	1.05	9558	0.004376	1.46	6856	0.022960	7.65	1306
Nursing Infants:								
0.000718	0.24	41763	0.001864	0.62	16097	0.006850	2.28	4379
Non-Nursing Infants:								
0.001937	0.65	15491	0.003279	1.09	9148	0.010721	3.57	2798
Female 13+ PREG:								
0.002314	0.77	12962	0.003022	1.01	9927	0.004593	1.53	6531
All Infants:								
0.001590	0.53	18869	0.002883	0.96	10407	0.010727	3.58	2796
Children 1-2:								
0.006880	2.29	4360	0.008848	2.95	3390	0.058481	19.49	512
Children 3-5:								
0.006608	2.20	4539	0.008646	2.88	3469	0.063933	21.31	469
Children 6-12:								
0.005202	1.73	5766	0.006886	2.30	4356	0.042088	14.03	712
Youth 13-19:								
0.003299	1.10	9094	0.004614	1.54	6501	0.021264	7.09	1410
Adults 20-49:								
0.002235	0.75	13422	0.002996	1.00	10013	0.020699	6.90	1449
Adults 50-99:								
0.001756	0.59	17080	0.002336	0.78	12841	0.007558	2.52	3969
Female 13-49:								
0.002202	0.73	13621	0.003096	1.03	9691	0.014050	4.68	2135
Custom demographics 1: Adults, 18+ yrs:								
0.002098	0.70	14296	0.002807	0.94	10685	0.016991	5.66	1765

Ver. 4.02, 05-10-c
DEEM-FCID ACUTE Analysis for DICROTOPHOS NHANES 2005-2010 2-Day
Residue file: dicrotophos acute food ppb.R10 Adjustment factor #2 NOT used.
Analysis Date: 12-14-2016/08:55:53 Residue file dated: 12-14-2016/08:53:14
NOEL (Acute) = 30.000000 mg/kg body-wt/day
RAC/FF intake summed over 24 hours
Run Comment: "Dose in ug/kg/day, Residue in ppb"
==========

Summary calculations--users:

--- 95th Percentile----			--- 97.5th Percentile----			---99.9th Percentile----		
Exposure	% aRfD	MOE	Exposure	% aRfD	MOE	Exposure	% aRfD	MOE
Total US Population:								
0.003191	1.06	9400	0.004434	1.48	6765	0.023056	7.69	1301
Nursing Infants:								
0.002949	0.98	10171	0.004236	1.41	7081	0.012289	4.10	2441
Non-Nursing Infants:								
0.004044	1.35	7418	0.005291	1.76	5669	0.010726	3.58	2797
Female 13+ PREG:								
0.002323	0.77	12915	0.003040	1.01	9868	0.004594	1.53	6530
All Infants:								
0.003691	1.23	8127	0.004611	1.54	6506	0.010766	3.59	2786
Children 1-2:								
0.007009	2.34	4280	0.008880	2.96	3378	0.079648	26.55	376
Children 3-5:								
0.006697	2.23	4479	0.008713	2.90	3443	0.063953	21.32	469
Children 6-12:								
0.005209	1.74	5759	0.006897	2.30	4349	0.042101	14.03	712
Youth 13-19:								
0.003325	1.11	9022	0.004638	1.55	6468	0.021279	7.09	1409
Adults 20-49:								
0.002268	0.76	13228	0.003026	1.01	9915	0.020719	6.91	1447
Adults 50-99:								
0.001768	0.59	16968	0.002349	0.78	12772	0.007566	2.52	3965
Female 13-49:								
0.002243	0.75	13377	0.003149	1.05	9526	0.015120	5.04	1984
Custom demographics 1: Adults, 18+ yrs:								
0.002114	0.70	14190	0.002823	0.94	10627	0.017040	5.68	1760

Ver. 4.02, 05-10-c
DEEM-FCID ACUTE Analysis for DICROTOPHOS NHANES 2005-2010 2-Day
Residue file: dicrotophos acute food ppb.R10 Adjustment factor #2 NOT used.
Analysis Date: 12-14-2016/08:55:53 Residue file dated: 12-14-2016/08:53:14
NOEL (Acute) = 30.000000 mg/kg body-wt/day
Acute Reference Dose (aRfD) = 0.300000 mg/kg body-wt/day
RAC/FF intake summed over 24 hours
Run Comment: "Dose in ug/kg/day, Residue in ppb"

Total US Population

	Daily Exposure Analysis /a (mg/kg body-weight/day) per Capita	per User
Mean	0.001024	0.001055
Standard Deviation	0.001900	0.001920
Standard Error of mean	0.000009	0.000009
Margin of Exposure 2/	29,294	28,432
Percent of aRfD	0.34	0.35

Percent of Person-Days that are User-Days = 97.06%

Estimated percentile of user-days falling below calculated exposure in mg/kg body-wt/day with Margin of Exposure (MOE) and Percent of aRfD

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
10.00	0.000110	0.04	273,362	90.00	0.002199	0.73	13,644
20.00	0.000217	0.07	138,126	95.00	0.003191	1.06	9,400
30.00	0.000341	0.11	87,865	97.50	0.004434	1.48	6,765
40.00	0.000480	0.16	62,448	99.00	0.006601	2.20	4,544
50.00	0.000637	0.21	47,129	99.50	0.009445	3.15	3,176
60.00	0.000823	0.27	36,460	99.75	0.015447	5.15	1,942
70.00	0.001082	0.36	27,738	99.90	0.023056	7.69	1,301
80.00	0.001459	0.49	20,561				

Estimated percentile of per-capita days falling below calculated exposure in mg/kg body-wt/day with Margin of Exposure (MOE) and Percent of aRfD

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
10.00	0.000084	0.03	359,260	90.00	0.002166	0.72	13,852
20.00	0.000189	0.06	158,439	95.00	0.003139	1.05	9,558
30.00	0.000314	0.10	95,609	97.50	0.004376	1.46	6,856
40.00	0.000453	0.15	66,194	99.00	0.006521	2.17	4,600
50.00	0.000612	0.20	48,990	99.50	0.009338	3.11	3,212
60.00	0.000797	0.27	37,637	99.75	0.015176	5.06	1,976
70.00	0.001053	0.35	28,482	99.90	0.022960	7.65	1,306
80.00	0.001430	0.48	20,975				

a/ Analysis based on all two-day participant records in NHANES 2005-2010 2-Day survey.
2/ Margin of Exposure = NOEL/ Dietary Exposure.

Ver. 4.02, 05-10-c
DEEM-FCID ACUTE Analysis for DICROTOPHOS NHANES 2005-2010 2-Day
Residue file: dicrotophos acute food ppb.R10 Adjustment factor #2 NOT used.
Analysis Date: 12-14-2016/08:55:53 Residue file dated: 12-14-2016/08:53:14
NOEL (Acute) = 30.000000 mg/kg body-wt/day
Acute Reference Dose (aRfD) = 0.300000 mg/kg body-wt/day
RAC/FF intake summed over 24 hours
Run Comment: "Dose in ug/kg/day, Residue in ppb"
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Nursing Infants

	Daily Exposure Analysis (mg/kg body-weight/day) per Capita	per User
Mean	0.000159	0.000671
Standard Deviation	0.000623	0.001139
Standard Error of mean	0.000023	0.000088
Margin of Exposure	189,235	44,722
Percent of aRfD	0.05	0.22

Percent of Person-Days that are User-Days = 23.63%

Estimated percentile of user-days falling below calculated exposure in mg/kg body-wt/day with Margin of Exposure (MOE) and Percent of aRfD

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
10.00	0.000013	0.00	>1,000,000	90.00	0.002066	0.69	14,520
20.00	0.000055	0.02	543,358	95.00	0.002949	0.98	10,171
30.00	0.000106	0.04	282,409	97.50	0.004236	1.41	7,081
40.00	0.000176	0.06	170,533	99.00	0.004550	1.52	6,593
50.00	0.000294	0.10	101,879	99.50	0.006841	2.28	4,385
60.00	0.000396	0.13	75,731	99.75	0.006871	2.29	4,366
70.00	0.000477	0.16	62,857	99.90	0.012289	4.10	2,441
80.00	0.000769	0.26	38,998				

Estimated percentile of per-capita days falling below calculated exposure in mg/kg body-wt/day with Margin of Exposure (MOE) and Percent of aRfD

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
10.00	0.000000	0.00	>1,000,000	90.00	0.000378	0.13	79,273
20.00	0.000000	0.00	>1,000,000	95.00	0.000718	0.24	41,763
30.00	0.000000	0.00	>1,000,000	97.50	0.001864	0.62	16,097
40.00	0.000000	0.00	>1,000,000	99.00	0.003029	1.01	9,903
50.00	0.000000	0.00	>1,000,000	99.50	0.004247	1.42	7,064
60.00	0.000000	0.00	>1,000,000	99.75	0.004541	1.51	6,606
70.00	0.000000	0.00	>1,000,000	99.90	0.006850	2.28	4,379
80.00	0.000028	0.01	>1,000,000				

Ver. 4.02, 05-10-c
DEEM-FCID ACUTE Analysis for DICROTOPHOS NHANES 2005-2010 2-Day
Residue file: dicrotophos acute food ppb.R10 Adjustment factor #2 NOT used.
Analysis Date: 12-14-2016/08:55:53 Residue file dated: 12-14-2016/08:53:14
NOEL (Acute) = 30.000000 mg/kg body-wt/day
Acute Reference Dose (aRfD) = 0.300000 mg/kg body-wt/day
RAC/FF intake summed over 24 hours
Run Comment: "Dose in ug/kg/day, Residue in ppb"
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Non-Nursing Infants

Daily Exposure Analysis (mg/kg body-weight/day)

	per Capita	per User
Mean	0.000374	0.000983
Standard Deviation	0.001060	0.001534
Standard Error of mean	0.000026	0.000061
Margin of Exposure	80,208	30,514
Percent of aRfD	0.12	0.33

Percent of Person-Days that are User-Days = 38.04%

Estimated percentile of user-days falling below calculated exposure in mg/kg body-wt/day with Margin of Exposure (MOE) and Percent of aRfD

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
10.00	0.000048	0.02	626,853	90.00	0.002443	0.81	12,280
20.00	0.000116	0.04	257,727	95.00	0.004044	1.35	7,418
30.00	0.000220	0.07	136,532	97.50	0.005291	1.76	5,669
40.00	0.000334	0.11	89,942	99.00	0.010124	3.37	2,963
50.00	0.000472	0.16	63,590	99.50	0.010715	3.57	2,799
60.00	0.000631	0.21	47,548	99.75	0.010722	3.57	2,798
70.00	0.000941	0.31	31,884	99.90	0.010726	3.58	2,797
80.00	0.001400	0.47	21,432				

Estimated percentile of per-capita days falling below calculated exposure in mg/kg body-wt/day with Margin of Exposure (MOE) and Percent of aRfD

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
10.00	0.000000	0.00	>1,000,000	90.00	0.001076	0.36	27,880
20.00	0.000000	0.00	>1,000,000	95.00	0.001937	0.65	15,491
30.00	0.000000	0.00	>1,000,000	97.50	0.003279	1.09	9,148
40.00	0.000000	0.00	>1,000,000	99.00	0.004905	1.63	6,116
50.00	0.000000	0.00	>1,000,000	99.50	0.009063	3.02	3,310
60.00	0.000000	0.00	>1,000,000	99.75	0.010710	3.57	2,801
70.00	0.000123	0.04	244,043	99.90	0.010721	3.57	2,798
80.00	0.000454	0.15	66,047				

Ver. 4.02, 05-10-c
DEEM-FCID ACUTE Analysis for DICROTOPHOS NHANES 2005-2010 2-Day
Residue file: dicrotophos acute food ppb.R10 Adjustment factor #2 NOT used.
Analysis Date: 12-14-2016/08:55:53 Residue file dated: 12-14-2016/08:53:14
NOEL (Acute) = 30.000000 mg/kg body-wt/day
Acute Reference Dose (aRfD) = 0.300000 mg/kg body-wt/day
RAC/FF intake summed over 24 hours
Run Comment: "Dose in ug/kg/day, Residue in ppb"
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Female 13+ PREG

	Daily Exposure Analysis (mg/kg body-weight/day) per Capita	per User
Mean	0.000878	0.000908
Standard Deviation	0.001410	0.001424
Standard Error of mean	0.000048	0.000049
Margin of Exposure	34,170	33,046
Percent of aRfD	0.29	0.30

Percent of Person-Days that are User-Days = 96.71%

Estimated percentile of user-days falling below calculated exposure in mg/kg body-wt/day with Margin of Exposure (MOE) and Percent of aRfD

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
10.00	0.000141	0.05	213,051	90.00	0.001876	0.63	15,989
20.00	0.000248	0.08	121,145	95.00	0.002323	0.77	12,915
30.00	0.000376	0.13	79,738	97.50	0.003040	1.01	9,868
40.00	0.000500	0.17	60,009	99.00	0.004356	1.45	6,887
50.00	0.000635	0.21	47,257	99.50	0.004542	1.51	6,605
60.00	0.000815	0.27	36,787	99.75	0.004575	1.53	6,556
70.00	0.001046	0.35	28,671	99.90	0.004594	1.53	6,530
80.00	0.001409	0.47	21,295				

Estimated percentile of per-capita days falling below calculated exposure in mg/kg body-wt/day with Margin of Exposure (MOE) and Percent of aRfD

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
10.00	0.000083	0.03	362,916	90.00	0.001871	0.62	16,037
20.00	0.000214	0.07	139,891	95.00	0.002314	0.77	12,962
30.00	0.000342	0.11	87,810	97.50	0.003022	1.01	9,927
40.00	0.000464	0.15	64,692	99.00	0.004354	1.45	6,890
50.00	0.000602	0.20	49,812	99.50	0.004538	1.51	6,610
60.00	0.000780	0.26	38,439	99.75	0.004574	1.52	6,558
70.00	0.001018	0.34	29,475	99.90	0.004593	1.53	6,531
80.00	0.001369	0.46	21,909				

Ver. 4.02, 05-10-c
DEEM-FCID ACUTE Analysis for DICROTOPHOS NHANES 2005-2010 2-Day
Residue file: dicrotophos acute food ppb.R10 Adjustment factor #2 NOT used.
Analysis Date: 12-14-2016/08:55:53 Residue file dated: 12-14-2016/08:53:14
NOEL (Acute) = 30.000000 mg/kg body-wt/day
Acute Reference Dose (aRfD) = 0.300000 mg/kg body-wt/day
RAC/FF intake summed over 24 hours
Run Comment: "Dose in ug/kg/day, Residue in ppb"
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All Infants

	Daily Exposure Analysis (mg/kg body-weight/day) per Capita	per User
Mean	0.000306	0.000914
Standard Deviation	0.000950	0.001461
Standard Error of mean	0.000019	0.000052
Margin of Exposure	97,961	32,827
Percent of aRfD	0.10	0.30

Percent of Person-Days that are User-Days = 33.51%

Estimated percentile of user-days falling below calculated exposure in mg/kg body-wt/day with Margin of Exposure (MOE) and Percent of aRfD

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
10.00	0.000040	0.01	748,951	90.00	0.002281	0.76	13,150
20.00	0.000106	0.04	283,452	95.00	0.003691	1.23	8,127
30.00	0.000185	0.06	162,323	97.50	0.004611	1.54	6,506
40.00	0.000292	0.10	102,716	99.00	0.009156	3.05	3,276
50.00	0.000423	0.14	70,864	99.50	0.010687	3.56	2,807
60.00	0.000569	0.19	52,730	99.75	0.010736	3.58	2,794
70.00	0.000827	0.28	36,280	99.90	0.010766	3.59	2,786
80.00	0.001328	0.44	22,586				

Estimated percentile of per-capita days falling below calculated exposure in mg/kg body-wt/day with Margin of Exposure (MOE) and Percent of aRfD

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
10.00	0.000000	0.00	>1,000,000	90.00	0.000830	0.28	36,147
20.00	0.000000	0.00	>1,000,000	95.00	0.001590	0.53	18,869
30.00	0.000000	0.00	>1,000,000	97.50	0.002883	0.96	10,407
40.00	0.000000	0.00	>1,000,000	99.00	0.004450	1.48	6,741
50.00	0.000000	0.00	>1,000,000	99.50	0.005367	1.79	5,589
60.00	0.000000	0.00	>1,000,000	99.75	0.010209	3.40	2,938
70.00	0.000043	0.01	699,198	99.90	0.010727	3.58	2,796
80.00	0.000301	0.10	99,743				

Ver. 4.02, 05-10-c
DEEM-FCID ACUTE Analysis for DICROTOPHOS NHANES 2005-2010 2-Day
Residue file: dicrotophos acute food ppb.R10 Adjustment factor #2 NOT used.
Analysis Date: 12-14-2016/08:55:53 Residue file dated: 12-14-2016/08:53:14
NOEL (Acute) = 30.000000 mg/kg body-wt/day
Acute Reference Dose (aRfD) = 0.300000 mg/kg body-wt/day
RAC/FF intake summed over 24 hours
Run Comment: "Dose in ug/kg/day, Residue in ppb"
==========

Children 1-2

	Daily Exposure Analysis (mg/kg body-weight/day) per Capita	per User
Mean	0.002469	0.002546
Standard Deviation	0.004368	0.004414
Standard Error of mean	0.000080	0.000083
Margin of Exposure	12,152	11,782
Percent of aRfD	0.82	0.85

Percent of Person-Days that are User-Days = 96.95%

Estimated percentile of user-days falling below calculated exposure in mg/kg body-wt/day with Margin of Exposure (MOE) and Percent of aRfD

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
10.00	0.000322	0.11	93,036	90.00	0.005240	1.75	5,724
20.00	0.000626	0.21	47,908	95.00	0.007009	2.34	4,280
30.00	0.000915	0.30	32,790	97.50	0.008880	2.96	3,378
40.00	0.001226	0.41	24,460	99.00	0.013543	4.51	2,215
50.00	0.001606	0.54	18,679	99.50	0.024481	8.16	1,225
60.00	0.002056	0.69	14,592	99.75	0.036149	12.05	829
70.00	0.002698	0.90	11,117	99.90	0.079648	26.55	376
80.00	0.003610	1.20	8,309				

Estimated percentile of per-capita days falling below calculated exposure in mg/kg body-wt/day with Margin of Exposure (MOE) and Percent of aRfD

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
10.00	0.000232	0.08	129,239	90.00	0.005160	1.72	5,813
20.00	0.000549	0.18	54,689	95.00	0.006880	2.29	4,360
30.00	0.000852	0.28	35,193	97.50	0.008848	2.95	3,390
40.00	0.001174	0.39	25,556	99.00	0.013467	4.49	2,227
50.00	0.001548	0.52	19,375	99.50	0.024455	8.15	1,226
60.00	0.001991	0.66	15,069	99.75	0.036077	12.03	831
70.00	0.002629	0.88	11,410	99.90	0.058481	19.49	512
80.00	0.003534	1.18	8,488				

Ver. 4.02, 05-10-c
DEEM-FCID ACUTE Analysis for DICROTOPHOS NHANES 2005-2010 2-Day
Residue file: dicrotophos acute food ppb.R10 Adjustment factor #2 NOT used.
Analysis Date: 12-14-2016/08:55:53 Residue file dated: 12-14-2016/08:53:14
NOEL (Acute) = 30.000000 mg/kg body-wt/day
Acute Reference Dose (aRfD) = 0.300000 mg/kg body-wt/day
RAC/FF intake summed over 24 hours
Run Comment: "Dose in ug/kg/day, Residue in ppb"
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Children 3-5

	Daily Exposure Analysis (mg/kg body-weight/day) per Capita	per User
Mean	0.002724	0.002762
Standard Deviation	0.004238	0.004256
Standard Error of mean	0.000080	0.000081
Margin of Exposure	11,014	10,861
Percent of aRfD	0.91	0.92

Percent of Person-Days that are User-Days = 98.61%

Estimated percentile of user-days falling below calculated exposure in mg/kg body-wt/day with Margin of Exposure (MOE) and Percent of aRfD

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
10.00	0.000475	0.16	63,129	90.00	0.005068	1.69	5,919
20.00	0.000822	0.27	36,493	95.00	0.006697	2.23	4,479
30.00	0.001210	0.40	24,783	97.50	0.008713	2.90	3,443
40.00	0.001618	0.54	18,536	99.00	0.018779	6.26	1,597
50.00	0.002023	0.67	14,832	99.50	0.021731	7.24	1,380
60.00	0.002513	0.84	11,937	99.75	0.048113	16.04	623
70.00	0.003026	1.01	9,913	99.90	0.063953	21.32	469
80.00	0.003732	1.24	8,038				

Estimated percentile of per-capita days falling below calculated exposure in mg/kg body-wt/day with Margin of Exposure (MOE) and Percent of aRfD

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
10.00	0.000418	0.14	71,786	90.00	0.005051	1.68	5,939
20.00	0.000763	0.25	39,307	95.00	0.006608	2.20	4,539
30.00	0.001176	0.39	25,505	97.50	0.008646	2.88	3,469
40.00	0.001572	0.52	19,082	99.00	0.018771	6.26	1,598
50.00	0.001997	0.67	15,024	99.50	0.021722	7.24	1,381
60.00	0.002490	0.83	12,045	99.75	0.048063	16.02	624
70.00	0.002989	1.00	10,035	99.90	0.063933	21.31	469
80.00	0.003709	1.24	8,087				

Ver. 4.02, 05-10-c
DEEM-FCID ACUTE Analysis for DICROTOPHOS NHANES 2005-2010 2-Day
Residue file: dicrotophos acute food ppb.R10 Adjustment factor #2 NOT used.
Analysis Date: 12-14-2016/08:55:53 Residue file dated: 12-14-2016/08:53:14
NOEL (Acute) = 30.000000 mg/kg body-wt/day
Acute Reference Dose (aRfD) = 0.300000 mg/kg body-wt/day
RAC/FF intake summed over 24 hours
Run Comment: "Dose in ug/kg/day, Residue in ppb"
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Children 6-12

	Daily Exposure Analysis (mg/kg body-weight/day) per Capita	per User
Mean	0.001972	0.001985
Standard Deviation	0.002831	0.002836
Standard Error of mean	0.000035	0.000035
Margin of Exposure	15,216	15,114
Percent of aRfD	0.66	0.66

Percent of Person-Days that are User-Days = 99.33%

Estimated percentile of user-days falling below calculated exposure in mg/kg body-wt/day with Margin of Exposure (MOE) and Percent of aRfD

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
10.00	0.000312	0.10	96,284	90.00	0.003770	1.26	7,958
20.00	0.000586	0.20	51,227	95.00	0.005209	1.74	5,759
30.00	0.000853	0.28	35,165	97.50	0.006897	2.30	4,349
40.00	0.001110	0.37	27,031	99.00	0.012066	4.02	2,486
50.00	0.001396	0.47	21,491	99.50	0.017725	5.91	1,692
60.00	0.001743	0.58	17,209	99.75	0.029170	9.72	1,028
70.00	0.002129	0.71	14,093	99.90	0.042101	14.03	712
80.00	0.002700	0.90	11,112				

Estimated percentile of per-capita days falling below calculated exposure in mg/kg body-wt/day with Margin of Exposure (MOE) and Percent of aRfD

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
10.00	0.000297	0.10	101,171	90.00	0.003748	1.25	8,005
20.00	0.000570	0.19	52,671	95.00	0.005202	1.73	5,766
30.00	0.000841	0.28	35,692	97.50	0.006886	2.30	4,356
40.00	0.001097	0.37	27,343	99.00	0.012056	4.02	2,488
50.00	0.001388	0.46	21,612	99.50	0.017520	5.84	1,712
60.00	0.001734	0.58	17,302	99.75	0.029155	9.72	1,028
70.00	0.002117	0.71	14,169	99.90	0.042088	14.03	712
80.00	0.002685	0.89	11,173				

Ver. 4.02, 05-10-c
DEEM-FCID ACUTE Analysis for DICROTOPHOS NHANES 2005-2010 2-Day
Residue file: dicrotophos acute food ppb.R10 Adjustment factor #2 NOT used.
Analysis Date: 12-14-2016/08:55:53 Residue file dated: 12-14-2016/08:53:14
NOEL (Acute) = 30.000000 mg/kg body-wt/day
Acute Reference Dose (aRfD) = 0.300000 mg/kg body-wt/day
RAC/FF intake summed over 24 hours
Run Comment: "Dose in ug/kg/day, Residue in ppb"
==========

Youth 13-19

	Daily Exposure Analysis (mg/kg body-weight/day) per Capita	per User
Mean	0.001209	0.001231
Standard Deviation	0.001794	0.001803
Standard Error of mean	0.000021	0.000022
Margin of Exposure	24,818	24,367
Percent of aRfD	0.40	0.41

Percent of Person-Days that are User-Days = 98.18%

Estimated percentile of user-days falling below calculated exposure in mg/kg body-wt/day with Margin of Exposure (MOE) and Percent of aRfD

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
10.00	0.000157	0.05	190,835	90.00	0.002375	0.79	12,632
20.00	0.000324	0.11	92,605	95.00	0.003325	1.11	9,022
30.00	0.000475	0.16	63,108	97.50	0.004638	1.55	6,468
40.00	0.000653	0.22	45,936	99.00	0.007132	2.38	4,206
50.00	0.000827	0.28	36,261	99.50	0.011822	3.94	2,537
60.00	0.001052	0.35	28,526	99.75	0.019017	6.34	1,577
70.00	0.001330	0.44	22,554	99.90	0.021279	7.09	1,409
80.00	0.001726	0.58	17,378				

Estimated percentile of per-capita days falling below calculated exposure in mg/kg body-wt/day with Margin of Exposure (MOE) and Percent of aRfD

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
10.00	0.000133	0.04	225,879	90.00	0.002353	0.78	12,752
20.00	0.000297	0.10	101,151	95.00	0.003299	1.10	9,094
30.00	0.000453	0.15	66,239	97.50	0.004614	1.54	6,501
40.00	0.000632	0.21	47,437	99.00	0.007107	2.37	4,221
50.00	0.000812	0.27	36,961	99.50	0.011814	3.94	2,539
60.00	0.001031	0.34	29,084	99.75	0.019011	6.34	1,578
70.00	0.001309	0.44	22,909	99.90	0.021264	7.09	1,410
80.00	0.001713	0.57	17,509				

Ver. 4.02, 05-10-c
DEEM-FCID ACUTE Analysis for DICROTOPHOS NHANES 2005-2010 2-Day
Residue file: dicrotophos acute food ppb.R10 Adjustment factor #2 NOT used.
Analysis Date: 12-14-2016/08:55:53 Residue file dated: 12-14-2016/08:53:14
NOEL (Acute) = 30.000000 mg/kg body-wt/day
Acute Reference Dose (aRfD) = 0.300000 mg/kg body-wt/day
RAC/FF intake summed over 24 hours
Run Comment: "Dose in ug/kg/day, Residue in ppb"
==========

Adults 20-49

	Daily Exposure Analysis (mg/kg body-weight/day) per Capita	per User
Mean	0.000828	0.000848
Standard Deviation	0.001358	0.001368
Standard Error of mean	0.000011	0.000012
Margin of Exposure	36,246	35,371
Percent of aRfD	0.28	0.28

Percent of Person-Days that are User-Days = 97.59%

Estimated percentile of user-days falling below calculated exposure in mg/kg body-wt/day with Margin of Exposure (MOE) and Percent of aRfD

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
10.00	0.000107	0.04	281,143	90.00	0.001707	0.57	17,577
20.00	0.000208	0.07	144,314	95.00	0.002268	0.76	13,228
30.00	0.000318	0.11	94,330	97.50	0.003026	1.01	9,915
40.00	0.000442	0.15	67,880	99.00	0.004352	1.45	6,894
50.00	0.000578	0.19	51,887	99.50	0.006222	2.07	4,821
60.00	0.000743	0.25	40,395	99.75	0.010138	3.38	2,959
70.00	0.000936	0.31	32,040	99.90	0.020719	6.91	1,447
80.00	0.001217	0.41	24,644				

Estimated percentile of per-capita days falling below calculated exposure in mg/kg body-wt/day with Margin of Exposure (MOE) and Percent of aRfD

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
10.00	0.000084	0.03	356,980	90.00	0.001691	0.56	17,742
20.00	0.000185	0.06	161,820	95.00	0.002235	0.75	13,422
30.00	0.000298	0.10	100,519	97.50	0.002996	1.00	10,013
40.00	0.000424	0.14	70,791	99.00	0.004324	1.44	6,937
50.00	0.000561	0.19	53,497	99.50	0.006106	2.04	4,913
60.00	0.000724	0.24	41,438	99.75	0.010105	3.37	2,968
70.00	0.000923	0.31	32,516	99.90	0.020699	6.90	1,449
80.00	0.001205	0.40	24,901				

Ver. 4.02, 05-10-c
DEEM-FCID ACUTE Analysis for DICROTOPHOS NHANES 2005-2010 2-Day
Residue file: dicrotophos acute food ppb.R10 Adjustment factor #2 NOT used.
Analysis Date: 12-14-2016/08:55:53 Residue file dated: 12-14-2016/08:53:14
NOEL (Acute) = 30.000000 mg/kg body-wt/day
Acute Reference Dose (aRfD) = 0.300000 mg/kg body-wt/day
RAC/FF intake summed over 24 hours
Run Comment: "Dose in ug/kg/day, Residue in ppb"
==========

Adults 50-99

	Daily Exposure Analysis (mg/kg body-weight/day) per Capita	per User
Mean	0.000624	0.000635
Standard Deviation	0.000735	0.000736
Standard Error of mean	0.000006	0.000006
Margin of Exposure	48,068	47,256
Percent of aRfD	0.21	0.21

Percent of Person-Days that are User-Days = 98.31%

Estimated percentile of user-days falling below calculated exposure in mg/kg body-wt/day with Margin of Exposure (MOE) and Percent of aRfD

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
10.00	0.000080	0.03	374,984	90.00	0.001379	0.46	21,761
20.00	0.000151	0.05	198,608	95.00	0.001768	0.59	16,968
30.00	0.000233	0.08	128,633	97.50	0.002349	0.78	12,772
40.00	0.000333	0.11	89,979	99.00	0.003219	1.07	9,320
50.00	0.000448	0.15	67,015	99.50	0.004281	1.43	7,008
60.00	0.000582	0.19	51,514	99.75	0.005797	1.93	5,175
70.00	0.000730	0.24	41,088	99.90	0.007566	2.52	3,965
80.00	0.000961	0.32	31,217				

Estimated percentile of per-capita days falling below calculated exposure in mg/kg body-wt/day with Margin of Exposure (MOE) and Percent of aRfD

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
10.00	0.000070	0.02	431,563	90.00	0.001367	0.46	21,953
20.00	0.000140	0.05	213,602	95.00	0.001756	0.59	17,080
30.00	0.000224	0.07	134,156	97.50	0.002336	0.78	12,841
40.00	0.000323	0.11	92,914	99.00	0.003153	1.05	9,515
50.00	0.000436	0.15	68,818	99.50	0.004268	1.42	7,029
60.00	0.000572	0.19	52,486	99.75	0.005787	1.93	5,183
70.00	0.000721	0.24	41,625	99.90	0.007558	2.52	3,969
80.00	0.000950	0.32	31,562				

Ver. 4.02, 05-10-c
DEEM-FCID ACUTE Analysis for DICROTOPHOS NHANES 2005-2010 2-Day
Residue file: dicrotophos acute food ppb.R10 Adjustment factor #2 NOT used.
Analysis Date: 12-14-2016/08:55:53 Residue file dated: 12-14-2016/08:53:14
NOEL (Acute) = 30.000000 mg/kg body-wt/day
Acute Reference Dose (aRfD) = 0.300000 mg/kg body-wt/day
RAC/FF intake summed over 24 hours
Run Comment: "Dose in ug/kg/day, Residue in ppb"
==========

Female 13-49

	Daily Exposure Analysis (mg/kg body-weight/day) per Capita	per User
Mean	0.000803	0.000825
Standard Deviation	0.001215	0.001224
Standard Error of mean	0.000012	0.000012
Margin of Exposure	37,372	36,366
Percent of aRfD	0.27	0.27

Percent of Person-Days that are User-Days = 97.31%

Estimated percentile of user-days falling below calculated exposure in mg/kg body-wt/day with Margin of Exposure (MOE) and Percent of aRfD

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
10.00	0.000102	0.03	294,248	90.00	0.001709	0.57	17,556
20.00	0.000195	0.07	153,735	95.00	0.002243	0.75	13,377
30.00	0.000304	0.10	98,639	97.50	0.003149	1.05	9,526
40.00	0.000422	0.14	71,163	99.00	0.004574	1.52	6,559
50.00	0.000554	0.18	54,110	99.50	0.005957	1.99	5,036
60.00	0.000715	0.24	41,945	99.75	0.008524	2.84	3,519
70.00	0.000913	0.30	32,846	99.90	0.015120	5.04	1,984
80.00	0.001205	0.40	24,892				

Estimated percentile of per-capita days falling below calculated exposure in mg/kg body-wt/day with Margin of Exposure (MOE) and Percent of aRfD

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
10.00	0.000081	0.03	368,471	90.00	0.001693	0.56	17,715
20.00	0.000171	0.06	175,493	95.00	0.002202	0.73	13,621
30.00	0.000282	0.09	106,453	97.50	0.003096	1.03	9,691
40.00	0.000404	0.13	74,268	99.00	0.004546	1.52	6,598
50.00	0.000532	0.18	56,361	99.50	0.005944	1.98	5,046
60.00	0.000694	0.23	43,221	99.75	0.008500	2.83	3,529
70.00	0.000891	0.30	33,668	99.90	0.014050	4.68	2,135
80.00	0.001185	0.39	25,323				

Ver. 4.02, 05-10-c
DEEM-FCID ACUTE Analysis for DICROTOPHOS NHANES 2005-2010 2-Day
Residue file: dicrotophos acute food ppb.R10 Adjustment factor #2 NOT used.
Analysis Date: 12-14-2016/08:55:53 Residue file dated: 12-14-2016/08:53:14
NOEL (Acute) = 30.000000 mg/kg body-wt/day
Acute Reference Dose (aRfD) = 0.300000 mg/kg body-wt/day
RAC/FF intake summed over 24 hours
Run Comment: "Dose in ug/kg/day, Residue in ppb"
==========

Custom demographics 1: Adults, 18+ yrs
Sex: M/F-all/
All Races
Age-Low: 18 yrs High: 99 yrs

	Daily Exposure Analysis (mg/kg body-weight/day) per Capita	per User
Mean	0.000755	0.000771
Standard Deviation	0.001161	0.001168
Standard Error of mean	0.000007	0.000007
Margin of Exposure	39,745	38,909
Percent of aRfD	0.25	0.26

Percent of Person-Days that are User-Days = 97.90%

Estimated percentile of user-days falling below calculated exposure
in mg/kg body-wt/day with Margin of Exposure (MOE) and Percent of aRfD

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
10.00	0.000093	0.03	323,254	90.00	0.001596	0.53	18,796
20.00	0.000181	0.06	165,367	95.00	0.002114	0.70	14,190
30.00	0.000284	0.09	105,813	97.50	0.002823	0.94	10,627
40.00	0.000397	0.13	75,536	99.00	0.004142	1.38	7,243
50.00	0.000527	0.18	56,952	99.50	0.005638	1.88	5,320
60.00	0.000673	0.22	44,556	99.75	0.008346	2.78	3,594
70.00	0.000856	0.29	35,040	99.90	0.017040	5.68	1,760
80.00	0.001128	0.38	26,598				

Estimated percentile of per-capita days falling below calculated exposure
in mg/kg body-wt/day with Margin of Exposure (MOE) and Percent of aRfD

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
10.00	0.000078	0.03	382,903	90.00	0.001582	0.53	18,959
20.00	0.000165	0.05	181,994	95.00	0.002098	0.70	14,296
30.00	0.000267	0.09	112,461	97.50	0.002807	0.94	10,685
40.00	0.000383	0.13	78,354	99.00	0.004126	1.38	7,271
50.00	0.000512	0.17	58,602	99.50	0.005617	1.87	5,341
60.00	0.000660	0.22	45,451	99.75	0.008115	2.70	3,696
70.00	0.000842	0.28	35,612	99.90	0.016991	5.66	1,765
80.00	0.001112	0.37	26,979				

Ver. 4.02, 05-10-c

DEEM-FCID Acute analysis for DICROTOPHOS
Residue file name: H:\MyFiles\DEEM-FCID Files\Dicrotophos\Dicrotophos v4.02 Files\dicrotophos acute food ppb.R10
Analysis Date 12-14-2016 Residue file dated: 12-14-2016/08:53:14
Reference dose: aRfD = 0.25 mg/kg bw/day NOEL = 25 mg/kg bw/day
Comment: Dose in ug/kg/day, Residue in ppb

EPA Code	Crop Grp	Food Name	Def Res (ppm)	Adj.Factors #1	#2	Comment
2003128000	20C	Cottonseed, oil	40.000000	1.000	1.000	residu
		Full comment: residue in ppb				
2003128001	20C	Cottonseed, oil-babyfood	40.000000	1.000	1.000	

Ver. 4.02, 05-10-c
DEEM-FCID ACUTE Analysis for DICROTOPHOS NHANES 2005-2010 2-Day
Residue file: dicrotophos acute food ppb.R10 Adjustment factor #2 NOT used.
Analysis Date: 12-14-2016/15:48:40 Residue file dated: 12-14-2016/08:53:14
NOEL (Acute) = 25.000000 mg/kg body-wt/day
Two-Day Average Results Reported
RAC/FF intake summed over 24 hours
Run Comment: "Dose in ug/kg/day, Residue in ppb"
==========

Summary calculations--per capita:

--- 95th Percentile----			--- 97.5th Percentile----			---99.9th Percentile----		
Exposure	% aRfD	MOE	Exposure	% aRfD	MOE	Exposure	% aRfD	MOE
Total US Population:								
0.002950	1.18	8475	0.003965	1.59	6305	0.018668	7.47	1339
Nursing Infants:								
0.000832	0.33	30042	0.001632	0.65	15314	0.004302	1.72	5811
Non-Nursing Infants:								
0.002133	0.85	11722	0.003025	1.21	8264	0.007393	2.96	3381
Female 13+ PREG:								
0.002153	0.86	11609	0.003016	1.21	8287	0.025786	10.31	969
All Infants:								
0.001596	0.64	15662	0.002856	1.14	8754	0.007393	2.96	3381
Children 1-2:								
0.006226	2.49	4015	0.008136	3.25	3072	0.041107	16.44	608
Children 3-5:								
0.006083	2.43	4109	0.009590	3.84	2606	0.042755	17.10	584
Children 6-12:								
0.004631	1.85	5398	0.006295	2.52	3971	0.026638	10.66	938
Youth 13-19:								
0.003019	1.21	8281	0.003918	1.57	6381	0.016049	6.42	1557
Adults 20-49:								
0.002043	0.82	12235	0.002590	1.04	9651	0.013006	5.20	1922
Adults 50-99:								
0.001606	0.64	15568	0.001965	0.79	12722	0.006727	2.69	3716
Female 13-49:								
0.002092	0.84	11950	0.002689	1.08	9296	0.012092	4.84	2067
Custom demographics 1: Adults, 18+ yrs:								
0.001912	0.76	13076	0.002437	0.97	10259	0.010571	4.23	2364

Ver. 4.02, 05-10-c
DEEM-FCID ACUTE Analysis for DICROTOPHOS NHANES 2005-2010 2-Day
Residue file: dicrotophos acute food ppb.R10 Adjustment factor #2 NOT used.
Analysis Date: 12-14-2016/15:48:40 Residue file dated: 12-14-2016/08:53:14
NOEL (Acute) = 25.000000 mg/kg body-wt/day
Two-Day Average Results Reported
RAC/FF intake summed over 24 hours
Run Comment: "Dose in ug/kg/day, Residue in ppb"
==========

Summary calculations--users:

--- 95th Percentile----			--- 97.5th Percentile----			---99.9th Percentile----		
Exposure	% aRfD	MOE	Exposure	% aRfD	MOE	Exposure	% aRfD	MOE
Total US Population:								
0.002963	1.19	8438	0.003976	1.59	6288	0.018680	7.47	1338
Nursing Infants:								
0.002186	0.87	11434	0.003987	1.59	6270	0.006612	2.64	3780
Non-Nursing Infants:								
0.003036	1.21	8233	0.004239	1.70	5897	0.007395	2.96	3380
Female 13+ PREG:								
0.002155	0.86	11602	0.003017	1.21	8287	0.025788	10.32	969
All Infants:								
0.003033	1.21	8241	0.003956	1.58	6318	0.007395	2.96	3380
Children 1-2:								
0.006237	2.49	4008	0.008156	3.26	3065	0.041110	16.44	608
Children 3-5:								
0.006087	2.43	4107	0.009601	3.84	2603	0.042756	17.10	584
Children 6-12:								
0.004631	1.85	5398	0.006295	2.52	3971	0.026638	10.66	938
Youth 13-19:								
0.003019	1.21	8281	0.003918	1.57	6380	0.016049	6.42	1557
Adults 20-49:								
0.002046	0.82	12218	0.002593	1.04	9640	0.013007	5.20	1922
Adults 50-99:								
0.001607	0.64	15561	0.001966	0.79	12719	0.006727	2.69	3716
Female 13-49:								
0.002098	0.84	11916	0.002701	1.08	9257	0.012094	4.84	2067
Custom demographics 1: Adults, 18+ yrs:								
0.001914	0.77	13061	0.002438	0.98	10253	0.010572	4.23	2364

Ver. 4.02, 05-10-c
DEEM-FCID ACUTE Analysis for DICROTOPHOS NHANES 2005-2010 2-Day
Residue file: dicrotophos acute food ppb.R10 Adjustment factor #2 NOT used.
Analysis Date: 12-14-2016/15:48:40 Residue file dated: 12-14-2016/08:53:14
NOEL (Acute) = 25.000000 mg/kg body-wt/day
Acute Reference Dose (aRfD) = 0.250000 mg/kg body-wt/day
Two-Day Average Results Reported
RAC/FF intake summed over 24 hours
Run Comment: "Dose in ug/kg/day, Residue in ppb"

Total US Population

2-Day Avg Exposure Analysis /a
(mg/kg body-weight/day)

	per Capita	per User
Mean	0.001024	0.001036
Standard Deviation	0.001482	0.001486
Standard Error of mean	0.000009	0.000010
Margin of Exposure 2/	24,412	24,125
Percent of aRfD	0.41	0.41

Percent of Individuals that are Users (over two days) = 98.83%

Estimated percentile of user-days falling below calculated exposure in mg/kg body-wt/day with Margin of Exposure (MOE) and Percent of aRfD

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
10.00	0.000185	0.07	134,926	90.00	0.002110	0.84	11,846
20.00	0.000308	0.12	81,268	95.00	0.002963	1.19	8,438
30.00	0.000424	0.17	58,928	97.50	0.003976	1.59	6,288
40.00	0.000544	0.22	45,968	99.00	0.005954	2.38	4,198
50.00	0.000681	0.27	36,696	99.50	0.008763	3.51	2,853
60.00	0.000850	0.34	29,394	99.75	0.011237	4.49	2,224
70.00	0.001072	0.43	23,318	99.90	0.018680	7.47	1,338
80.00	0.001409	0.56	17,740				

Estimated percentile of per-capita days falling below calculated exposure in mg/kg body-wt/day with Margin of Exposure (MOE) and Percent of aRfD

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
10.00	0.000171	0.07	146,243	90.00	0.002097	0.84	11,920
20.00	0.000297	0.12	84,296	95.00	0.002950	1.18	8,475
30.00	0.000415	0.17	60,206	97.50	0.003965	1.59	6,305
40.00	0.000536	0.21	46,646	99.00	0.005927	2.37	4,217
50.00	0.000674	0.27	37,116	99.50	0.008706	3.48	2,871
60.00	0.000843	0.34	29,659	99.75	0.011151	4.46	2,241
70.00	0.001062	0.42	23,531	99.90	0.018668	7.47	1,339
80.00	0.001400	0.56	17,851				

a/ Analysis based on all two-day participant records in NHANES 2005-2010 2-Day survey.
2/ Margin of Exposure = NOEL/ Dietary Exposure.

Ver. 4.02, 05-10-c
DEEM-FCID ACUTE Analysis for DICROTOPHOS NHANES 2005-2010 2-Day
Residue file: dicrotophos acute food ppb.R10 Adjustment factor #2 NOT used.
Analysis Date: 12-14-2016/15:48:40 Residue file dated: 12-14-2016/08:53:14
NOEL (Acute) = 25.000000 mg/kg body-wt/day
Acute Reference Dose (aRfD) = 0.250000 mg/kg body-wt/day
Two-Day Average Results Reported
RAC/FF intake summed over 24 hours
Run Comment: "Dose in ug/kg/day, Residue in ppb"
==========

Nursing Infants

2-Day Avg Exposure Analysis
(mg/kg body-weight/day)

	per Capita	per User
Mean	0.000159	0.000544
Standard Deviation	0.000544	0.000898
Standard Error of mean	0.000028	0.000087
Margin of Exposure	157,696	45,988
Percent of aRfD	0.06	0.22

Percent of Individuals that are Users (over two days) = 29.16%

Estimated percentile of user-days falling below calculated exposure
in mg/kg body-wt/day with Margin of Exposure (MOE) and Percent of aRfD

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
10.00	0.000010	0.00	>1,000,000	90.00	0.001627	0.65	15,365
20.00	0.000030	0.01	827,758	95.00	0.002186	0.87	11,434
30.00	0.000105	0.04	237,893	97.50	0.003987	1.59	6,270
40.00	0.000165	0.07	151,180	99.00	0.004271	1.71	5,853
50.00	0.000209	0.08	119,584	99.50	0.004294	1.72	5,821
60.00	0.000278	0.11	90,042	99.75	0.004306	1.72	5,805
70.00	0.000404	0.16	61,957	99.90	0.006612	2.64	3,780
80.00	0.000741	0.30	33,746				

Estimated percentile of per-capita days falling below calculated exposure
in mg/kg body-wt/day with Margin of Exposure (MOE) and Percent of aRfD

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
10.00	0.000000	0.00	>1,000,000	90.00	0.000373	0.15	67,086
20.00	0.000000	0.00	>1,000,000	95.00	0.000832	0.33	30,042
30.00	0.000000	0.00	>1,000,000	97.50	0.001632	0.65	15,314
40.00	0.000000	0.00	>1,000,000	99.00	0.003277	1.31	7,629
50.00	0.000000	0.00	>1,000,000	99.50	0.004004	1.60	6,243
60.00	0.000000	0.00	>1,000,000	99.75	0.004278	1.71	5,844
70.00	0.000000	0.00	>1,000,000	99.90	0.004302	1.72	5,811
80.00	0.000108	0.04	230,464				

Ver. 4.02, 05-10-c
DEEM-FCID ACUTE Analysis for DICROTOPHOS NHANES 2005-2010 2-Day
Residue file: dicrotophos acute food ppb.R10 Adjustment factor #2 NOT used.
Analysis Date: 12-14-2016/15:48:40 Residue file dated: 12-14-2016/08:53:14
NOEL (Acute) = 25.000000 mg/kg body-wt/day
Acute Reference Dose (aRfD) = 0.250000 mg/kg body-wt/day
Two-Day Average Results Reported
RAC/FF intake summed over 24 hours
Run Comment: "Dose in ug/kg/day, Residue in ppb"

Non-Nursing Infants

2-Day Avg Exposure Analysis (mg/kg body-weight/day)

	per Capita	per User
Mean	0.000374	0.000819
Standard Deviation	0.000937	0.001249
Standard Error of mean	0.000033	0.000063
Margin of Exposure	66,840	30,536
Percent of aRfD	0.15	0.33

Percent of Individuals that are Users (over two days) = 45.69%

Estimated percentile of user-days falling below calculated exposure in mg/kg body-wt/day with Margin of Exposure (MOE) and Percent of aRfD

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
10.00	0.000043	0.02	578,932	90.00	0.002227	0.89	11,224
20.00	0.000105	0.04	238,811	95.00	0.003036	1.21	8,233
30.00	0.000185	0.07	134,890	97.50	0.004239	1.70	5,897
40.00	0.000281	0.11	89,050	99.00	0.007383	2.95	3,385
50.00	0.000412	0.16	60,697	99.50	0.007390	2.96	3,383
60.00	0.000552	0.22	45,282	99.75	0.007393	2.96	3,381
70.00	0.000776	0.31	32,230	99.90	0.007395	2.96	3,380
80.00	0.001124	0.45	22,233				

Estimated percentile of per-capita days falling below calculated exposure in mg/kg body-wt/day with Margin of Exposure (MOE) and Percent of aRfD

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
10.00	0.000000	0.00	>1,000,000	90.00	0.001017	0.41	24,572
20.00	0.000000	0.00	>1,000,000	95.00	0.002133	0.85	11,722
30.00	0.000000	0.00	>1,000,000	97.50	0.003025	1.21	8,264
40.00	0.000000	0.00	>1,000,000	99.00	0.005898	2.36	4,238
50.00	0.000000	0.00	>1,000,000	99.50	0.007382	2.95	3,386
60.00	0.000052	0.02	482,702	99.75	0.007389	2.96	3,383
70.00	0.000221	0.09	112,881	99.90	0.007393	2.96	3,381
80.00	0.000474	0.19	52,700				

Ver. 4.02, 05-10-c
DEEM-FCID ACUTE Analysis for DICROTOPHOS NHANES 2005-2010 2-Day
Residue file: dicrotophos acute food ppb.R10 Adjustment factor #2 NOT used.
Analysis Date: 12-14-2016/15:48:40 Residue file dated: 12-14-2016/08:53:14
NOEL (Acute) = 25.000000 mg/kg body-wt/day
Acute Reference Dose (aRfD) = 0.250000 mg/kg body-wt/day
Two-Day Average Results Reported
RAC/FF intake summed over 24 hours
Run Comment: "Dose in ug/kg/day, Residue in ppb"
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Female 13+ PREG

2-Day Avg Exposure Analysis
(mg/kg body-weight/day)

	per Capita	per User
Mean	0.000878	0.000884
Standard Deviation	0.001053	0.001054
Standard Error of mean	0.000051	0.000051
Margin of Exposure	28,475	28,283
Percent of aRfD	0.35	0.35

Percent of Individuals that are Users (over two days) = 99.33%

Estimated percentile of user-days falling below calculated exposure in mg/kg body-wt/day with Margin of Exposure (MOE) and Percent of aRfD

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
10.00	0.000183	0.07	136,984	90.00	0.001608	0.64	15,549
20.00	0.000334	0.13	74,829	95.00	0.002155	0.86	11,602
30.00	0.000483	0.19	51,722	97.50	0.003017	1.21	8,287
40.00	0.000580	0.23	43,073	99.00	0.003205	1.28	7,800
50.00	0.000714	0.29	35,033	99.50	0.003862	1.54	6,472
60.00	0.000827	0.33	30,240	99.75	0.003884	1.55	6,436
70.00	0.000976	0.39	25,602	99.90	0.025788	10.32	969
80.00	0.001302	0.52	19,207				

Estimated percentile of per-capita days falling below calculated exposure in mg/kg body-wt/day with Margin of Exposure (MOE) and Percent of aRfD

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
10.00	0.000181	0.07	138,454	90.00	0.001607	0.64	15,555
20.00	0.000332	0.13	75,376	95.00	0.002153	0.86	11,609
30.00	0.000481	0.19	52,000	97.50	0.003016	1.21	8,287
40.00	0.000578	0.23	43,287	99.00	0.003205	1.28	7,800
50.00	0.000711	0.28	35,165	99.50	0.003862	1.54	6,473
60.00	0.000825	0.33	30,285	99.75	0.003884	1.55	6,436
70.00	0.000970	0.39	25,763	99.90	0.025786	10.31	969
80.00	0.001300	0.52	19,229				

Ver. 4.02, 05-10-c
DEEM-FCID ACUTE Analysis for DICROTOPHOS NHANES 2005-2010 2-Day
Residue file: dicrotophos acute food ppb.R10 Adjustment factor #2 NOT used.
Analysis Date: 12-14-2016/15:48:40 Residue file dated: 12-14-2016/08:53:14
NOEL (Acute) = 25.000000 mg/kg body-wt/day
Acute Reference Dose (aRfD) = 0.250000 mg/kg body-wt/day
Two-Day Average Results Reported
RAC/FF intake summed over 24 hours
Run Comment: "Dose in ug/kg/day, Residue in ppb"
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All Infants

2-Day Avg Exposure Analysis
(mg/kg body-weight/day)

	per Capita	per User
Mean	0.000306	0.000756
Standard Deviation	0.000840	0.001184
Standard Error of mean	0.000024	0.000053
Margin of Exposure	81,634	33,052
Percent of aRfD	0.12	0.30

Percent of Individuals that are Users (over two days) = 40.49%

Estimated percentile of user-days falling below calculated exposure
in mg/kg body-wt/day with Margin of Exposure (MOE) and Percent of aRfD

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
10.00	0.000026	0.01	949,486	90.00	0.001898	0.76	13,173
20.00	0.000092	0.04	270,418	95.00	0.003033	1.21	8,241
30.00	0.000161	0.06	155,716	97.50	0.003956	1.58	6,318
40.00	0.000240	0.10	103,987	99.00	0.006747	2.70	3,705
50.00	0.000337	0.13	74,091	99.50	0.007390	2.96	3,383
60.00	0.000471	0.19	53,126	99.75	0.007393	2.96	3,381
70.00	0.000694	0.28	36,001	99.90	0.007395	2.96	3,380
80.00	0.001111	0.44	22,504				

Estimated percentile of per-capita days falling below calculated exposure
in mg/kg body-wt/day with Margin of Exposure (MOE) and Percent of aRfD

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
10.00	0.000000	0.00	>1,000,000	90.00	0.000861	0.34	29,035
20.00	0.000000	0.00	>1,000,000	95.00	0.001596	0.64	15,662
30.00	0.000000	0.00	>1,000,000	97.50	0.002856	1.14	8,754
40.00	0.000000	0.00	>1,000,000	99.00	0.003959	1.58	6,314
50.00	0.000000	0.00	>1,000,000	99.50	0.006721	2.69	3,719
60.00	0.000003	0.00	>1,000,000	99.75	0.007388	2.96	3,383
70.00	0.000124	0.05	201,123	99.90	0.007393	2.96	3,381
80.00	0.000350	0.14	71,396				

Ver. 4.02, 05-10-c
DEEM-FCID ACUTE Analysis for DICROTOPHOS NHANES 2005-2010 2-Day
Residue file: dicrotophos acute food ppb.R10 Adjustment factor #2 NOT used.
Analysis Date: 12-14-2016/15:48:40 Residue file dated: 12-14-2016/08:53:14
NOEL (Acute) = 25.000000 mg/kg body-wt/day
Acute Reference Dose (aRfD) = 0.250000 mg/kg body-wt/day
Two-Day Average Results Reported
RAC/FF intake summed over 24 hours
Run Comment: "Dose in ug/kg/day, Residue in ppb"
==========

Children 1-2

2-Day Avg Exposure Analysis
(mg/kg body-weight/day)

	per Capita	per User
Mean	0.002469	0.002490
Standard Deviation	0.003364	0.003370
Standard Error of mean	0.000087	0.000088
Margin of Exposure	10,127	10,039
Percent of aRfD	0.99	1.00

Percent of Individuals that are Users (over two days) = 99.13%

Estimated percentile of user-days falling below calculated exposure in mg/kg body-wt/day with Margin of Exposure (MOE) and Percent of aRfD

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
10.00	0.000533	0.21	46,931	90.00	0.004830	1.93	5,175
20.00	0.000800	0.32	31,254	95.00	0.006237	2.49	4,008
30.00	0.001076	0.43	23,229	97.50	0.008156	3.26	3,065
40.00	0.001389	0.56	18,002	99.00	0.013182	5.27	1,896
50.00	0.001767	0.71	14,145	99.50	0.018674	7.47	1,338
60.00	0.002164	0.87	11,553	99.75	0.033639	13.46	743
70.00	0.002709	1.08	9,227	99.90	0.041110	16.44	608
80.00	0.003424	1.37	7,300				

Estimated percentile of per-capita days falling below calculated exposure in mg/kg body-wt/day with Margin of Exposure (MOE) and Percent of aRfD

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
10.00	0.000495	0.20	50,499	90.00	0.004818	1.93	5,189
20.00	0.000787	0.31	31,760	95.00	0.006226	2.49	4,015
30.00	0.001062	0.42	23,545	97.50	0.008136	3.25	3,072
40.00	0.001379	0.55	18,122	99.00	0.013178	5.27	1,897
50.00	0.001721	0.69	14,529	99.50	0.018663	7.47	1,339
60.00	0.002152	0.86	11,615	99.75	0.033634	13.45	743
70.00	0.002698	1.08	9,264	99.90	0.041107	16.44	608
80.00	0.003405	1.36	7,342				

Ver. 4.02, 05-10-c
DEEM-FCID ACUTE Analysis for DICROTOPHOS NHANES 2005-2010 2-Day
Residue file: dicrotophos acute food ppb.R10 Adjustment factor #2 NOT used.
Analysis Date: 12-14-2016/15:48:40 Residue file dated: 12-14-2016/08:53:14
NOEL (Acute) = 25.000000 mg/kg body-wt/day
Acute Reference Dose (aRfD) = 0.250000 mg/kg body-wt/day
Two-Day Average Results Reported
RAC/FF intake summed over 24 hours
Run Comment: "Dose in ug/kg/day, Residue in ppb"
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Children 3-5

2-Day Avg Exposure Analysis
(mg/kg body-weight/day)

	per Capita	per User
Mean	0.002724	0.002730
Standard Deviation	0.003133	0.003133
Standard Error of mean	0.000083	0.000083
Margin of Exposure	9,178	9,158
Percent of aRfD	1.09	1.09

Percent of Individuals that are Users (over two days) = 99.78%

Estimated percentile of user-days falling below calculated exposure in mg/kg body-wt/day with Margin of Exposure (MOE) and Percent of aRfD

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
10.00	0.000780	0.31	32,037	90.00	0.004496	1.80	5,559
20.00	0.001121	0.45	22,306	95.00	0.006087	2.43	4,107
30.00	0.001501	0.60	16,655	97.50	0.009601	3.84	2,603
40.00	0.001829	0.73	13,669	99.00	0.011694	4.68	2,137
50.00	0.002156	0.86	11,593	99.50	0.024881	9.95	1,004
60.00	0.002547	1.02	9,815	99.75	0.034589	13.84	722
70.00	0.002936	1.17	8,515	99.90	0.042756	17.10	584
80.00	0.003604	1.44	6,936				

Estimated percentile of per-capita days falling below calculated exposure in mg/kg body-wt/day with Margin of Exposure (MOE) and Percent of aRfD

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
10.00	0.000770	0.31	32,465	90.00	0.004493	1.80	5,563
20.00	0.001116	0.45	22,402	95.00	0.006083	2.43	4,109
30.00	0.001494	0.60	16,734	97.50	0.009590	3.84	2,606
40.00	0.001826	0.73	13,688	99.00	0.011693	4.68	2,137
50.00	0.002150	0.86	11,629	99.50	0.024877	9.95	1,004
60.00	0.002545	1.02	9,823	99.75	0.034587	13.83	722
70.00	0.002933	1.17	8,524	99.90	0.042755	17.10	584
80.00	0.003601	1.44	6,941				

DEEM-FCID ACUTE Analysis for DICROTOPHOS NHANES 2005-2010 2-Day
Residue file: dicrotophos acute food ppb.R10 Adjustment factor #2 NOT used.
Analysis Date: 12-14-2016/15:48:40 Residue file dated: 12-14-2016/08:53:14
NOEL (Acute) = 25.000000 mg/kg body-wt/day
Acute Reference Dose (aRfD) = 0.250000 mg/kg body-wt/day
Two-Day Average Results Reported
RAC/FF intake summed over 24 hours
Run Comment: "Dose in ug/kg/day, Residue in ppb"

Children 6-12

2-Day Avg Exposure Analysis
(mg/kg body-weight/day)

	per Capita	per User
Mean	0.001972	0.001972
Standard Deviation	0.002161	0.002161
Standard Error of mean	0.000038	0.000038
Margin of Exposure	12,680	12,675
Percent of aRfD	0.79	0.79

Percent of Individuals that are Users (over two days) = 99.96%

Estimated percentile of user-days falling below calculated exposure in mg/kg body-wt/day with Margin of Exposure (MOE) and Percent of aRfD

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
10.00	0.000530	0.21	47,172	90.00	0.003574	1.43	6,995
20.00	0.000772	0.31	32,368	95.00	0.004631	1.85	5,398
30.00	0.001004	0.40	24,890	97.50	0.006295	2.52	3,971
40.00	0.001232	0.49	20,288	99.00	0.009866	3.95	2,533
50.00	0.001501	0.60	16,651	99.50	0.017412	6.96	1,435
60.00	0.001788	0.72	13,985	99.75	0.020783	8.31	1,202
70.00	0.002162	0.86	11,563	99.90	0.026638	10.66	938
80.00	0.002663	1.07	9,387				

Estimated percentile of per-capita days falling below calculated exposure in mg/kg body-wt/day with Margin of Exposure (MOE) and Percent of aRfD

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
10.00	0.000528	0.21	47,326	90.00	0.003573	1.43	6,996
20.00	0.000772	0.31	32,393	95.00	0.004631	1.85	5,398
30.00	0.001004	0.40	24,912	97.50	0.006295	2.52	3,971
40.00	0.001232	0.49	20,297	99.00	0.009865	3.95	2,534
50.00	0.001501	0.60	16,658	99.50	0.017411	6.96	1,435
60.00	0.001787	0.71	13,988	99.75	0.020782	8.31	1,202
70.00	0.002161	0.86	11,566	99.90	0.026638	10.66	938
80.00	0.002663	1.07	9,389				

Ver. 4.02, 05-10-c
DEEM-FCID ACUTE Analysis for DICROTOPHOS NHANES 2005-2010 2-Day
Residue file: dicrotophos acute food ppb.R10 Adjustment factor #2 NOT used.
Analysis Date: 12-14-2016/15:48:40 Residue file dated: 12-14-2016/08:53:14
NOEL (Acute) = 25.000000 mg/kg body-wt/day
Acute Reference Dose (aRfD) = 0.250000 mg/kg body-wt/day
Two-Day Average Results Reported
RAC/FF intake summed over 24 hours
Run Comment: "Dose in ug/kg/day, Residue in ppb"
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Youth 13-19

2-Day Avg Exposure Analysis
(mg/kg body-weight/day)

	per Capita	per User
Mean	0.001209	0.001209
Standard Deviation	0.001332	0.001332
Standard Error of mean	0.000023	0.000023
Margin of Exposure	20,681	20,678
Percent of aRfD	0.48	0.48

Percent of Individuals that are Users (over two days) = 99.99%

Estimated percentile of user-days falling below calculated exposure in mg/kg body-wt/day with Margin of Exposure (MOE) and Percent of aRfD

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
10.00	0.000272	0.11	91,856	90.00	0.002324	0.93	10,759
20.00	0.000437	0.17	57,153	95.00	0.003019	1.21	8,281
30.00	0.000571	0.23	43,765	97.50	0.003918	1.57	6,380
40.00	0.000754	0.30	33,148	99.00	0.005989	2.40	4,174
50.00	0.000925	0.37	27,013	99.50	0.009579	3.83	2,609
60.00	0.001105	0.44	22,634	99.75	0.010256	4.10	2,437
70.00	0.001327	0.53	18,839	99.90	0.016049	6.42	1,557
80.00	0.001621	0.65	15,419				

Estimated percentile of per-capita days falling below calculated exposure in mg/kg body-wt/day with Margin of Exposure (MOE) and Percent of aRfD

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
10.00	0.000272	0.11	91,964	90.00	0.002323	0.93	10,759
20.00	0.000437	0.17	57,175	95.00	0.003019	1.21	8,281
30.00	0.000571	0.23	43,780	97.50	0.003918	1.57	6,381
40.00	0.000754	0.30	33,154	99.00	0.005989	2.40	4,174
50.00	0.000925	0.37	27,017	99.50	0.009579	3.83	2,609
60.00	0.001104	0.44	22,635	99.75	0.010256	4.10	2,437
70.00	0.001327	0.53	18,841	99.90	0.016049	6.42	1,557
80.00	0.001621	0.65	15,420				

Ver. 4.02, 05-10-c
DEEM-FCID ACUTE Analysis for DICROTOPHOS NHANES 2005-2010 2-Day
Residue file: dicrotophos acute food ppb.R10 Adjustment factor #2 NOT used.
Analysis Date: 12-14-2016/15:48:40 Residue file dated: 12-14-2016/08:53:14
NOEL (Acute) = 25.000000 mg/kg body-wt/day
Acute Reference Dose (aRfD) = 0.250000 mg/kg body-wt/day
Two-Day Average Results Reported
RAC/FF intake summed over 24 hours
Run Comment: "Dose in ug/kg/day, Residue in ppb"
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Adults 20-49

2-Day Avg Exposure Analysis
(mg/kg body-weight/day)

	per Capita	per User
Mean	0.000828	0.000831
Standard Deviation	0.001002	0.001002
Standard Error of mean	0.000012	0.000012
Margin of Exposure	30,205	30,084
Percent of aRfD	0.33	0.33

Percent of Individuals that are Users (over two days) = 99.60%

Estimated percentile of user-days falling below calculated exposure
in mg/kg body-wt/day with Margin of Exposure (MOE) and Percent of aRfD

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
10.00	0.000184	0.07	135,505	90.00	0.001551	0.62	16,118
20.00	0.000299	0.12	83,716	95.00	0.002046	0.82	12,218
30.00	0.000408	0.16	61,261	97.50	0.002593	1.04	9,640
40.00	0.000516	0.21	48,491	99.00	0.003800	1.52	6,578
50.00	0.000628	0.25	39,796	99.50	0.005807	2.32	4,305
60.00	0.000768	0.31	32,551	99.75	0.009999	4.00	2,500
70.00	0.000930	0.37	26,882	99.90	0.013007	5.20	1,922
80.00	0.001159	0.46	21,561				

Estimated percentile of per-capita days falling below calculated exposure
in mg/kg body-wt/day with Margin of Exposure (MOE) and Percent of aRfD

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
10.00	0.000181	0.07	138,346	90.00	0.001549	0.62	16,136
20.00	0.000296	0.12	84,599	95.00	0.002043	0.82	12,235
30.00	0.000405	0.16	61,708	97.50	0.002590	1.04	9,651
40.00	0.000512	0.20	48,789	99.00	0.003789	1.52	6,597
50.00	0.000626	0.25	39,915	99.50	0.005804	2.32	4,307
60.00	0.000766	0.31	32,643	99.75	0.009646	3.86	2,591
70.00	0.000928	0.37	26,939	99.90	0.013006	5.20	1,922
80.00	0.001158	0.46	21,596				

Ver. 4.02, 05-10-c
DEEM-FCID ACUTE Analysis for DICROTOPHOS NHANES 2005-2010 2-Day
Residue file: dicrotophos acute food ppb.R10 Adjustment factor #2 NOT used.
Analysis Date: 12-14-2016/15:48:40 Residue file dated: 12-14-2016/08:53:14
NOEL (Acute) = 25.000000 mg/kg body-wt/day
Acute Reference Dose (aRfD) = 0.250000 mg/kg body-wt/day
Two-Day Average Results Reported
RAC/FF intake summed over 24 hours
Run Comment: "Dose in ug/kg/day, Residue in ppb"
==========

Adults 50-99

2-Day Avg Exposure Analysis
(mg/kg body-weight/day)

	per Capita	per User
Mean	0.000624	0.000625
Standard Deviation	0.000589	0.000589
Standard Error of mean	0.000007	0.000007
Margin of Exposure	40,057	40,002
Percent of aRfD	0.25	0.25

Percent of Individuals that are Users (over two days) = 99.86%

Estimated percentile of user-days falling below calculated exposure
in mg/kg body-wt/day with Margin of Exposure (MOE) and Percent of aRfD

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
10.00	0.000138	0.06	181,124	90.00	0.001250	0.50	19,994
20.00	0.000225	0.09	111,221	95.00	0.001607	0.64	15,561
30.00	0.000308	0.12	81,237	97.50	0.001966	0.79	12,719
40.00	0.000395	0.16	63,235	99.00	0.002804	1.12	8,914
50.00	0.000484	0.19	51,648	99.50	0.003570	1.43	7,003
60.00	0.000587	0.23	42,586	99.75	0.004058	1.62	6,160
70.00	0.000719	0.29	34,758	99.90	0.006727	2.69	3,716
80.00	0.000905	0.36	27,630				

Estimated percentile of per-capita days falling below calculated exposure
in mg/kg body-wt/day with Margin of Exposure (MOE) and Percent of aRfD

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
10.00	0.000137	0.05	182,902	90.00	0.001249	0.50	20,008
20.00	0.000224	0.09	111,638	95.00	0.001606	0.64	15,568
30.00	0.000307	0.12	81,475	97.50	0.001965	0.79	12,722
40.00	0.000395	0.16	63,311	99.00	0.002804	1.12	8,917
50.00	0.000483	0.19	51,729	99.50	0.003569	1.43	7,003
60.00	0.000586	0.23	42,628	99.75	0.004058	1.62	6,160
70.00	0.000719	0.29	34,783	99.90	0.006727	2.69	3,716
80.00	0.000904	0.36	27,663				

DEEM-FCID ACUTE Analysis for DICROTOPHOS NHANES 2005-2010 2-Day
Residue file: dicrotophos acute food ppb.R10 Adjustment factor #2 NOT used.
Analysis Date: 12-14-2016/15:48:40 Residue file dated: 12-14-2016/08:53:14
NOEL (Acute) = 25.000000 mg/kg body-wt/day
Acute Reference Dose (aRfD) = 0.250000 mg/kg body-wt/day
Two-Day Average Results Reported
RAC/FF intake summed over 24 hours
Run Comment: "Dose in ug/kg/day, Residue in ppb"

Female 13-49

2-Day Avg Exposure Analysis
(mg/kg body-weight/day)

	per Capita	per User
Mean	0.000803	0.000807
Standard Deviation	0.000919	0.000919
Standard Error of mean	0.000012	0.000012
Margin of Exposure	31,143	30,981
Percent of aRfD	0.32	0.32

Percent of Individuals that are Users (over two days) = 99.48%

Estimated percentile of user-days falling below calculated exposure in mg/kg body-wt/day with Margin of Exposure (MOE) and Percent of aRfD

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
10.00	0.000176	0.07	142,381	90.00	0.001548	0.62	16,153
20.00	0.000284	0.11	88,139	95.00	0.002098	0.84	11,916
30.00	0.000387	0.15	64,525	97.50	0.002701	1.08	9,257
40.00	0.000488	0.20	51,260	99.00	0.003694	1.48	6,768
50.00	0.000607	0.24	41,153	99.50	0.004863	1.95	5,140
60.00	0.000741	0.30	33,726	99.75	0.006482	2.59	3,856
70.00	0.000922	0.37	27,106	99.90	0.012094	4.84	2,067
80.00	0.001128	0.45	22,158				

Estimated percentile of per-capita days falling below calculated exposure in mg/kg body-wt/day with Margin of Exposure (MOE) and Percent of aRfD

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
10.00	0.000169	0.07	147,640	90.00	0.001545	0.62	16,177
20.00	0.000279	0.11	89,721	95.00	0.002092	0.84	11,950
30.00	0.000384	0.15	65,179	97.50	0.002689	1.08	9,296
40.00	0.000484	0.19	51,704	99.00	0.003686	1.47	6,781
50.00	0.000605	0.24	41,348	99.50	0.004861	1.94	5,142
60.00	0.000739	0.30	33,850	99.75	0.006478	2.59	3,859
70.00	0.000920	0.37	27,183	99.90	0.012092	4.84	2,067
80.00	0.001120	0.45	22,316				

Ver. 4.02, 05-10-c
DEEM-FCID ACUTE Analysis for DICROTOPHOS NHANES 2005-2010 2-Day
Residue file: dicrotophos acute food ppb.R10 Adjustment factor #2 NOT used.
Analysis Date: 12-14-2016/15:48:40 Residue file dated: 12-14-2016/08:53:14
NOEL (Acute) = 25.000000 mg/kg body-wt/day
Acute Reference Dose (aRfD) = 0.250000 mg/kg body-wt/day
Two-Day Average Results Reported
RAC/FF intake summed over 24 hours
Run Comment: "Dose in ug/kg/day, Residue in ppb"
==========

Custom demographics 1: Adults, 18+ yrs
Sex: M/F-all/
All Races
Age-Low: 18 yrs High: 99 yrs

	2-Day Avg Exposure Analysis (mg/kg body-weight/day) per Capita	per User
Mean	0.000755	0.000757
Standard Deviation	0.000871	0.000871
Standard Error of mean	0.000007	0.000007
Margin of Exposure	33,121	33,028
Percent of aRfD	0.30	0.30

Percent of Individuals that are Users (over two days) = 99.72%

Estimated percentile of user-days falling below calculated exposure
in mg/kg body-wt/day with Margin of Exposure (MOE) and Percent of aRfD

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
10.00	0.000162	0.06	154,072	90.00	0.001458	0.58	17,145
20.00	0.000266	0.11	94,158	95.00	0.001914	0.77	13,061
30.00	0.000367	0.15	68,155	97.50	0.002438	0.98	10,253
40.00	0.000464	0.19	53,884	99.00	0.003516	1.41	7,109
50.00	0.000570	0.23	43,847	99.50	0.004574	1.83	5,466
60.00	0.000692	0.28	36,151	99.75	0.007723	3.09	3,237
70.00	0.000850	0.34	29,420	99.90	0.010572	4.23	2,364
80.00	0.001070	0.43	23,362				

Estimated percentile of per-capita days falling below calculated exposure
in mg/kg body-wt/day with Margin of Exposure (MOE) and Percent of aRfD

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
10.00	0.000160	0.06	156,336	90.00	0.001456	0.58	17,164
20.00	0.000263	0.11	95,122	95.00	0.001912	0.76	13,076
30.00	0.000365	0.15	68,504	97.50	0.002437	0.97	10,259
40.00	0.000463	0.19	54,053	99.00	0.003513	1.41	7,115
50.00	0.000569	0.23	43,973	99.50	0.004571	1.83	5,468
60.00	0.000690	0.28	36,238	99.75	0.007719	3.09	3,238
70.00	0.000848	0.34	29,469	99.90	0.010571	4.23	2,364
80.00	0.001068	0.43	23,405				

Ver. 4.02, 05-10-c

DEEM-FCID Acute analysis for DICROTOPHOS
Residue file name: H:\MyFiles\DEEM-FCID Files\Dicrotophos\Dicrotophos v4.02 Files\Dicrotophos acute water ppb.R10
Analysis Date 12-14-2016 Residue file dated: 12-14-2016/08:40:13
Reference dose: aRfD = 0.3 mg/kg bw/day NOEL = 30 mg/kg bw/day
Comment: Dose in ug/kg/day, Residue in ppb

RDL indices and parameters for Monte Carlo Analysis:

Index #	Dist Code	Parameter #1	Param #2	Param #3	Comment
1	6	Drinking Water ppb.rdf			

EPA Code	Crop Grp	Food Name	Def Res (ppm)	Adj.Factors #1	#2	RDL Pntr	Comment
8601000000	86A	Water, direct, all sources	0.009000	1.000	1.000	1	residu
Full comment: residue in ppb							
8602000000	86B	Water, indirect, all sources	0.009000	1.000	1.000	1	residu
Full comment: residue in ppb							

Summary of Residue Distribution Files (RDF) listed in H:\MyFiles\DEEM-FCID Files\Dicrotophos\Dicrotophos v4.02 Files\Dicrotophos acute water ppb.R10

RDF #	File Name	N residues w freq's	N residues w/o freq's	N LODs	LOD Value	N Zeros
1	Drinking Water ppb.rdf	0	400	0	0	0

Ver. 4.02, 05-10-c
DEEM-FCID ACUTE Analysis for DICROTOPHOS NHANES 2005-2010 2-Day
Residue file: Dicrotophos acute water ppb.R10 Adjustment factor #2 NOT used.
Analysis Date: 12-14-2016/08:44:20 Residue file dated: 12-14-2016/08:40:13
NOEL (Acute) = 30.000000 mg/kg body-wt/day
RAC/FF intake summed over 24 hours
MC iterations = 100; MC list in residue file; MC seed = 1; RNG = MS VB
Run Comment: "Dose in ug/kg/day, Residue in ppb"
==========

Summary calculations--per capita:

--- 95th Percentile----			--- 97.5th Percentile----			---99.9th Percentile----		
Exposure	% aRfD	MOE	Exposure	% aRfD	MOE	Exposure	% aRfD	MOE
Total US Population:								
0.000327	0.11	91736	0.000426	0.14	70351	0.001156	0.39	25951
Nursing Infants:								
0.000590	0.20	50852	0.000747	0.25	40172	0.002166	0.72	13847
Non-Nursing Infants:								
0.001282	0.43	23394	0.001518	0.51	19763	0.002643	0.88	11349
Female 13+ PREG:								
0.000327	0.11	91738	0.000383	0.13	78417	0.000636	0.21	47202
All Infants:								
0.001175	0.39	25523	0.001403	0.47	21382	0.002367	0.79	12671
Children 1-2:								
0.000470	0.16	63790	0.000583	0.19	51467	0.001668	0.56	17985
Children 3-5:								
0.000375	0.13	79917	0.000470	0.16	63889	0.001043	0.35	28760
Children 6-12:								
0.000289	0.10	103682	0.000377	0.13	79589	0.000904	0.30	33194
Youth 13-19:								
0.000268	0.09	112035	0.000343	0.11	87584	0.000754	0.25	39777
Adults 20-49:								
0.000324	0.11	92640	0.000404	0.13	74190	0.000818	0.27	36652
Adults 50-99:								
0.000288	0.10	104044	0.000352	0.12	85309	0.000748	0.25	40125
Female 13-49:								
0.000326	0.11	92035	0.000405	0.14	74001	0.000800	0.27	37520
Custom demographics 1: Adults, 18+ yrs:								
0.000308	0.10	97286	0.000383	0.13	78323	0.000776	0.26	38657

Ver. 4.02, 05-10-c
DEEM-FCID ACUTE Analysis for DICROTOPHOS NHANES 2005-2010 2-Day
Residue file: Dicrotophos acute water ppb.R10 Adjustment factor #2 NOT used.
Analysis Date: 12-14-2016/08:44:20 Residue file dated: 12-14-2016/08:40:13
NOEL (Acute) = 30.000000 mg/kg body-wt/day
RAC/FF intake summed over 24 hours
MC iterations = 100; MC list in residue file; MC seed = 1; RNG = MS VB
Run Comment: "Dose in ug/kg/day, Residue in ppb"
==========

Summary calculations--users:

--- 95th Percentile----			--- 97.5th Percentile----			---99.9th Percentile----		
Exposure	% aRfD	MOE	Exposure	% aRfD	MOE	Exposure	% aRfD	MOE
Total US Population:								
0.000333	0.11	90026	0.000433	0.14	69286	0.001168	0.39	25679
Nursing Infants:								
0.000726	0.24	41296	0.000909	0.30	32987	0.002176	0.73	13788
Non-Nursing Infants:								
0.001290	0.43	23264	0.001523	0.51	19695	0.002646	0.88	11339
Female 13+ PREG:								
0.000330	0.11	90921	0.000384	0.13	78173	0.000652	0.22	46043
All Infants:								
0.001230	0.41	24397	0.001463	0.49	20507	0.002628	0.88	11416
Children 1-2:								
0.000482	0.16	62278	0.000596	0.20	50366	0.001686	0.56	17789
Children 3-5:								
0.000383	0.13	78395	0.000481	0.16	62405	0.001069	0.36	28067
Children 6-12:								
0.000298	0.10	100619	0.000393	0.13	76407	0.000917	0.31	32707
Youth 13-19:								
0.000277	0.09	108469	0.000352	0.12	85239	0.000785	0.26	38215
Adults 20-49:								
0.000328	0.11	91527	0.000409	0.14	73304	0.000824	0.27	36389
Adults 50-99:								
0.000290	0.10	103488	0.000353	0.12	85019	0.000749	0.25	40079
Female 13-49:								
0.000332	0.11	90347	0.000411	0.14	72905	0.000809	0.27	37086
Custom demographics 1: Adults, 18+ yrs:								
0.000311	0.10	96349	0.000386	0.13	77627	0.000781	0.26	38422

Ver. 4.02, 05-10-c
DEEM-FCID ACUTE Analysis for DICROTOPHOS NHANES 2005-2010 2-Day
Residue file: Dicrotophos acute water ppb.R10 Adjustment factor #2 NOT used.
Analysis Date: 12-14-2016/08:44:20 Residue file dated: 12-14-2016/08:40:13
NOEL (Acute) = 30.000000 mg/kg body-wt/day
Acute Reference Dose (aRfD) = 0.300000 mg/kg body-wt/day
RAC/FF intake summed over 24 hours
MC iterations = 100; MC list in residue file; MC seed = 1; RNG = MS VB
Run Comment: "Dose in ug/kg/day, Residue in ppb"

Total US Population	Daily Exposure Analysis /a (mg/kg body-weight/day) per Capita	per User
Mean	0.000106	0.000111
Standard Deviation	0.000128	0.000129
Margin of Exposure 2/	282,887	270,506
Percent of aRfD	0.04	0.04

Percent of Person-Days that are User-Days = 95.62%

Estimated percentile of user-days falling below calculated exposure in mg/kg body-wt/day with Margin of Exposure (MOE) and Percent of aRfD

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
10.00	0.000009	0.00	>1,000,000	90.00	0.000251	0.08	119,580
20.00	0.000019	0.01	>1,000,000	95.00	0.000333	0.11	90,026
30.00	0.000031	0.01	955,329	97.50	0.000433	0.14	69,286
40.00	0.000050	0.02	595,332	99.00	0.000598	0.20	50,202
50.00	0.000074	0.02	402,878	99.50	0.000742	0.25	40,409
60.00	0.000101	0.03	296,922	99.75	0.000933	0.31	32,169
70.00	0.000134	0.04	224,558	99.90	0.001168	0.39	25,679
80.00	0.000177	0.06	169,679				

Estimated percentile of per-capita days falling below calculated exposure in mg/kg body-wt/day with Margin of Exposure (MOE) and Percent of aRfD

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
10.00	0.000006	0.00	>1,000,000	90.00	0.000246	0.08	121,858
20.00	0.000015	0.00	>1,000,000	95.00	0.000327	0.11	91,736
30.00	0.000027	0.01	>1,000,000	97.50	0.000426	0.14	70,351
40.00	0.000045	0.01	671,916	99.00	0.000589	0.20	50,975
50.00	0.000069	0.02	436,066	99.50	0.000730	0.24	41,097
60.00	0.000096	0.03	312,426	99.75	0.000919	0.31	32,627
70.00	0.000129	0.04	233,426	99.90	0.001156	0.39	25,951
80.00	0.000172	0.06	174,258				

a/ Analysis based on all two-day participant records in NHANES 2005-2010 2-Day with 2 days of valid drinking water records.
2/ Margin of Exposure = NOEL/ Dietary Exposure.

Ver. 4.02, 05-10-c
DEEM-FCID ACUTE Analysis for DICROTOPHOS NHANES 2005-2010 2-Day
Residue file: Dicrotophos acute water ppb.R10 Adjustment factor #2 NOT used.
Analysis Date: 12-14-2016/08:44:20 Residue file dated: 12-14-2016/08:40:13
NOEL (Acute) = 30.000000 mg/kg body-wt/day
Acute Reference Dose (aRfD) = 0.300000 mg/kg body-wt/day
RAC/FF intake summed over 24 hours
MC iterations = 100; MC list in residue file; MC seed = 1; RNG = MS VB
Run Comment: "Dose in ug/kg/day, Residue in ppb"
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Nursing Infants

	Daily Exposure Analysis (mg/kg body-weight/day) per Capita	per User
Mean	0.000120	0.000209
Standard Deviation	0.000234	0.000277
Margin of Exposure	249,726	143,259
Percent of aRfD	0.04	0.07

Percent of Person-Days that are User-Days = 57.37%

Estimated percentile of user-days falling below calculated exposure in mg/kg body-wt/day with Margin of Exposure (MOE) and Percent of aRfD

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
10.00	0.000010	0.00	>1,000,000	90.00	0.000562	0.19	53,393
20.00	0.000021	0.01	>1,000,000	95.00	0.000726	0.24	41,296
30.00	0.000042	0.01	708,836	97.50	0.000909	0.30	32,987
40.00	0.000071	0.02	423,401	99.00	0.001260	0.42	23,811
50.00	0.000100	0.03	299,111	99.50	0.001551	0.52	19,337
60.00	0.000153	0.05	195,509	99.75	0.002093	0.70	14,330
70.00	0.000225	0.07	133,410	99.90	0.002176	0.73	13,788
80.00	0.000369	0.12	81,297				

Estimated percentile of per-capita days falling below calculated exposure in mg/kg body-wt/day with Margin of Exposure (MOE) and Percent of aRfD

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
10.00	0.000000	0.00	>1,000,000	90.00	0.000422	0.14	71,020
20.00	0.000000	0.00	>1,000,000	95.00	0.000590	0.20	50,852
30.00	0.000000	0.00	>1,000,000	97.50	0.000747	0.25	40,172
40.00	0.000000	0.00	>1,000,000	99.00	0.000995	0.33	30,154
50.00	0.000012	0.00	>1,000,000	99.50	0.001327	0.44	22,602
60.00	0.000043	0.01	700,138	99.75	0.001706	0.57	17,585
70.00	0.000095	0.03	315,461	99.90	0.002166	0.72	13,847
80.00	0.000185	0.06	161,820				

Ver. 4.02, 05-10-c
DEEM-FCID ACUTE Analysis for DICROTOPHOS NHANES 2005-2010 2-Day
Residue file: Dicrotophos acute water ppb.R10 Adjustment factor #2 NOT used.
Analysis Date: 12-14-2016/08:44:20 Residue file dated: 12-14-2016/08:40:13
NOEL (Acute) = 30.000000 mg/kg body-wt/day
Acute Reference Dose (aRfD) = 0.300000 mg/kg body-wt/day
RAC/FF intake summed over 24 hours
MC iterations = 100; MC list in residue file; MC seed = 1; RNG = MS VB
Run Comment: "Dose in ug/kg/day, Residue in ppb"
==========

Non-Nursing Infants

	Daily Exposure Analysis (mg/kg body-weight/day) per Capita	per User
Mean	0.000524	0.000539
Standard Deviation	0.000424	0.000421
Margin of Exposure	57,271	55,666
Percent of aRfD	0.17	0.18

Percent of Person-Days that are User-Days = 97.20%

Estimated percentile of user-days falling below calculated exposure in mg/kg body-wt/day with Margin of Exposure (MOE) and Percent of aRfD

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
10.00	0.000071	0.02	420,815	90.00	0.001080	0.36	27,785
20.00	0.000108	0.04	276,854	95.00	0.001290	0.43	23,264
30.00	0.000187	0.06	160,699	97.50	0.001523	0.51	19,695
40.00	0.000383	0.13	78,407	99.00	0.001780	0.59	16,850
50.00	0.000513	0.17	58,432	99.50	0.002027	0.68	14,802
60.00	0.000615	0.20	48,804	99.75	0.002254	0.75	13,309
70.00	0.000723	0.24	41,483	99.90	0.002646	0.88	11,339
80.00	0.000862	0.29	34,787				

Estimated percentile of per-capita days falling below calculated exposure in mg/kg body-wt/day with Margin of Exposure (MOE) and Percent of aRfD

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
10.00	0.000060	0.02	498,229	90.00	0.001074	0.36	27,944
20.00	0.000098	0.03	305,978	95.00	0.001282	0.43	23,394
30.00	0.000163	0.05	184,191	97.50	0.001518	0.51	19,763
40.00	0.000353	0.12	84,929	99.00	0.001777	0.59	16,880
50.00	0.000496	0.17	60,479	99.50	0.002020	0.67	14,853
60.00	0.000601	0.20	49,899	99.75	0.002249	0.75	13,338
70.00	0.000716	0.24	41,908	99.90	0.002643	0.88	11,349
80.00	0.000854	0.28	35,109				

Ver. 4.02, 05-10-c
DEEM-FCID ACUTE Analysis for DICROTOPHOS NHANES 2005-2010 2-Day
Residue file: Dicrotophos acute water ppb.R10 Adjustment factor #2 NOT used.
Analysis Date: 12-14-2016/08:44:20 Residue file dated: 12-14-2016/08:40:13
NOEL (Acute) = 30.000000 mg/kg body-wt/day
Acute Reference Dose (aRfD) = 0.300000 mg/kg body-wt/day
RAC/FF intake summed over 24 hours
MC iterations = 100; MC list in residue file; MC seed = 1; RNG = MS VB
Run Comment: "Dose in ug/kg/day, Residue in ppb"
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Female 13+ PREG

	Daily Exposure Analysis (mg/kg body-weight/day) per Capita	per User
Mean	0.000111	0.000114
Standard Deviation	0.000109	0.000109
Margin of Exposure	271,007	262,386
Percent of aRfD	0.04	0.04

Percent of Person-Days that are User-Days = 96.82%

Estimated percentile of user-days falling below calculated exposure in mg/kg body-wt/day with Margin of Exposure (MOE) and Percent of aRfD

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
10.00	0.000011	0.00	>1,000,000	90.00	0.000274	0.09	109,308
20.00	0.000021	0.01	>1,000,000	95.00	0.000330	0.11	90,921
30.00	0.000038	0.01	786,124	97.50	0.000384	0.13	78,173
40.00	0.000058	0.02	519,158	99.00	0.000460	0.15	65,233
50.00	0.000083	0.03	359,438	99.50	0.000499	0.17	60,087
60.00	0.000107	0.04	279,936	99.75	0.000546	0.18	54,994
70.00	0.000143	0.05	209,225	99.90	0.000652	0.22	46,043
80.00	0.000199	0.07	150,568				

Estimated percentile of per-capita days falling below calculated exposure in mg/kg body-wt/day with Margin of Exposure (MOE) and Percent of aRfD

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
10.00	0.000008	0.00	>1,000,000	90.00	0.000272	0.09	110,437
20.00	0.000018	0.01	>1,000,000	95.00	0.000327	0.11	91,738
30.00	0.000034	0.01	871,846	97.50	0.000383	0.13	78,417
40.00	0.000052	0.02	578,924	99.00	0.000459	0.15	65,384
50.00	0.000079	0.03	379,791	99.50	0.000496	0.17	60,466
60.00	0.000104	0.03	288,370	99.75	0.000544	0.18	55,173
70.00	0.000139	0.05	215,727	99.90	0.000636	0.21	47,202
80.00	0.000194	0.06	154,376				

Ver. 4.02, 05-10-c
DEEM-FCID ACUTE Analysis for DICROTOPHOS NHANES 2005-2010 2-Day
Residue file: Dicrotophos acute water ppb.R10 Adjustment factor #2 NOT used.
Analysis Date: 12-14-2016/08:44:20 Residue file dated: 12-14-2016/08:40:13
NOEL (Acute) = 30.000000 mg/kg body-wt/day
Acute Reference Dose (aRfD) = 0.300000 mg/kg body-wt/day
RAC/FF intake summed over 24 hours
MC iterations = 100; MC list in residue file; MC seed = 1; RNG = MS VB
Run Comment: "Dose in ug/kg/day, Residue in ppb"
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All Infants

	Daily Exposure Analysis (mg/kg body-weight/day) per Capita	per User
Mean	0.000397	0.000469
Standard Deviation	0.000419	0.000417
Margin of Exposure	75,597	64,007
Percent of aRfD	0.13	0.16

Percent of Person-Days that are User-Days = 84.67%

Estimated percentile of user-days falling below calculated exposure in mg/kg body-wt/day with Margin of Exposure (MOE) and Percent of aRfD

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
10.00	0.000044	0.01	683,807	90.00	0.001024	0.34	29,291
20.00	0.000083	0.03	362,553	95.00	0.001230	0.41	24,397
30.00	0.000125	0.04	240,470	97.50	0.001463	0.49	20,507
40.00	0.000230	0.08	130,570	99.00	0.001760	0.59	17,048
50.00	0.000403	0.13	74,492	99.50	0.001953	0.65	15,362
60.00	0.000533	0.18	56,337	99.75	0.002206	0.74	13,598
70.00	0.000648	0.22	46,319	99.90	0.002628	0.88	11,416
80.00	0.000794	0.26	37,776				

Estimated percentile of per-capita days falling below calculated exposure in mg/kg body-wt/day with Margin of Exposure (MOE) and Percent of aRfD

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
10.00	0.000000	0.00	>1,000,000	90.00	0.000976	0.33	30,747
20.00	0.000020	0.01	>1,000,000	95.00	0.001175	0.39	25,523
30.00	0.000074	0.02	407,075	97.50	0.001403	0.47	21,382
40.00	0.000119	0.04	251,132	99.00	0.001702	0.57	17,624
50.00	0.000247	0.08	121,691	99.50	0.001885	0.63	15,918
60.00	0.000440	0.15	68,123	99.75	0.002168	0.72	13,835
70.00	0.000584	0.19	51,361	99.90	0.002367	0.79	12,671
80.00	0.000741	0.25	40,494				

Ver. 4.02, 05-10-c
DEEM-FCID ACUTE Analysis for DICROTOPHOS NHANES 2005-2010 2-Day
Residue file: Dicrotophos acute water ppb.R10 Adjustment factor #2 NOT used.
Analysis Date: 12-14-2016/08:44:20 Residue file dated: 12-14-2016/08:40:13
NOEL (Acute) = 30.000000 mg/kg body-wt/day
Acute Reference Dose (aRfD) = 0.300000 mg/kg body-wt/day
RAC/FF intake summed over 24 hours
MC iterations = 100; MC list in residue file; MC seed = 1; RNG = MS VB
Run Comment: "Dose in ug/kg/day, Residue in ppb"
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Children 1-2

	Daily Exposure Analysis (mg/kg body-weight/day) per Capita	per User
Mean	0.000146	0.000156
Standard Deviation	0.000176	0.000177
Margin of Exposure	205,186	192,232
Percent of aRfD	0.05	0.05

Percent of Person-Days that are User-Days = 93.69%

Estimated percentile of user-days falling below calculated exposure in mg/kg body-wt/day with Margin of Exposure (MOE) and Percent of aRfD

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
10.00	0.000012	0.00	>1,000,000	90.00	0.000366	0.12	82,071
20.00	0.000024	0.01	>1,000,000	95.00	0.000482	0.16	62,278
30.00	0.000042	0.01	714,608	97.50	0.000596	0.20	50,366
40.00	0.000068	0.02	439,446	99.00	0.000759	0.25	39,533
50.00	0.000101	0.03	295,915	99.50	0.000910	0.30	32,980
60.00	0.000142	0.05	211,260	99.75	0.001106	0.37	27,129
70.00	0.000191	0.06	157,332	99.90	0.001686	0.56	17,789
80.00	0.000258	0.09	116,312				

Estimated percentile of per-capita days falling below calculated exposure in mg/kg body-wt/day with Margin of Exposure (MOE) and Percent of aRfD

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
10.00	0.000005	0.00	>1,000,000	90.00	0.000356	0.12	84,247
20.00	0.000017	0.01	>1,000,000	95.00	0.000470	0.16	63,790
30.00	0.000033	0.01	906,944	97.50	0.000583	0.19	51,467
40.00	0.000056	0.02	533,172	99.00	0.000745	0.25	40,279
50.00	0.000090	0.03	334,073	99.50	0.000883	0.29	33,990
60.00	0.000130	0.04	230,338	99.75	0.001076	0.36	27,891
70.00	0.000180	0.06	167,018	99.90	0.001668	0.56	17,985
80.00	0.000247	0.08	121,574				

Ver. 4.02, 05-10-c
DEEM-FCID ACUTE Analysis for DICROTOPHOS NHANES 2005-2010 2-Day
Residue file: Dicrotophos acute water ppb.R10 Adjustment factor #2 NOT used.
Analysis Date: 12-14-2016/08:44:20 Residue file dated: 12-14-2016/08:40:13
NOEL (Acute) = 30.000000 mg/kg body-wt/day
Acute Reference Dose (aRfD) = 0.300000 mg/kg body-wt/day
RAC/FF intake summed over 24 hours
MC iterations = 100; MC list in residue file; MC seed = 1; RNG = MS VB
Run Comment: "Dose in ug/kg/day, Residue in ppb"
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Children 3-5

	Daily Exposure Analysis (mg/kg body-weight/day) per Capita	per User
Mean	0.000119	0.000127
Standard Deviation	0.000136	0.000136
Margin of Exposure	252,988	237,149
Percent of aRfD	0.04	0.04

Percent of Person-Days that are User-Days = 93.74%

Estimated percentile of user-days falling below calculated exposure in mg/kg body-wt/day with Margin of Exposure (MOE) and Percent of aRfD

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
10.00	0.000010	0.00	>1,000,000	90.00	0.000294	0.10	101,909
20.00	0.000020	0.01	>1,000,000	95.00	0.000383	0.13	78,395
30.00	0.000036	0.01	843,745	97.50	0.000481	0.16	62,405
40.00	0.000057	0.02	530,082	99.00	0.000622	0.21	48,265
50.00	0.000084	0.03	358,745	99.50	0.000742	0.25	40,452
60.00	0.000119	0.04	252,652	99.75	0.000894	0.30	33,562
70.00	0.000158	0.05	190,468	99.90	0.001069	0.36	28,067
80.00	0.000211	0.07	142,213				

Estimated percentile of per-capita days falling below calculated exposure in mg/kg body-wt/day with Margin of Exposure (MOE) and Percent of aRfD

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
10.00	0.000004	0.00	>1,000,000	90.00	0.000287	0.10	104,517
20.00	0.000015	0.00	>1,000,000	95.00	0.000375	0.13	79,917
30.00	0.000027	0.01	>1,000,000	97.50	0.000470	0.16	63,889
40.00	0.000046	0.02	648,668	99.00	0.000612	0.20	49,023
50.00	0.000074	0.02	406,201	99.50	0.000731	0.24	41,049
60.00	0.000109	0.04	276,485	99.75	0.000889	0.30	33,733
70.00	0.000151	0.05	199,024	99.90	0.001043	0.35	28,760
80.00	0.000202	0.07	148,360				

Ver. 4.02, 05-10-c
DEEM-FCID ACUTE Analysis for DICROTOPHOS NHANES 2005-2010 2-Day
Residue file: Dicrotophos acute water ppb.R10 Adjustment factor #2 NOT used.
Analysis Date: 12-14-2016/08:44:20 Residue file dated: 12-14-2016/08:40:13
NOEL (Acute) = 30.000000 mg/kg body-wt/day
Acute Reference Dose (aRfD) = 0.300000 mg/kg body-wt/day
RAC/FF intake summed over 24 hours
MC iterations = 100; MC list in residue file; MC seed = 1; RNG = MS VB
Run Comment: "Dose in ug/kg/day, Residue in ppb"
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Children 6-12

	Daily Exposure Analysis (mg/kg body-weight/day) per Capita	per User
Mean	0.000088	0.000096
Standard Deviation	0.000110	0.000111
Margin of Exposure	339,999	313,944
Percent of aRfD	0.03	0.03

Percent of Person-Days that are User-Days = 92.34%

Estimated percentile of user-days falling below calculated exposure in mg/kg body-wt/day with Margin of Exposure (MOE) and Percent of aRfD

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
10.00	0.000007	0.00	>1,000,000	90.00	0.000223	0.07	134,334
20.00	0.000015	0.00	>1,000,000	95.00	0.000298	0.10	100,619
30.00	0.000025	0.01	>1,000,000	97.50	0.000393	0.13	76,407
40.00	0.000040	0.01	743,137	99.00	0.000525	0.17	57,180
50.00	0.000060	0.02	498,017	99.50	0.000619	0.21	48,460
60.00	0.000085	0.03	354,104	99.75	0.000729	0.24	41,143
70.00	0.000115	0.04	260,509	99.90	0.000917	0.31	32,707
80.00	0.000156	0.05	192,077				

Estimated percentile of per-capita days falling below calculated exposure in mg/kg body-wt/day with Margin of Exposure (MOE) and Percent of aRfD

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
10.00	0.000002	0.00	>1,000,000	90.00	0.000214	0.07	139,982
20.00	0.000010	0.00	>1,000,000	95.00	0.000289	0.10	103,682
30.00	0.000019	0.01	>1,000,000	97.50	0.000377	0.13	79,589
40.00	0.000032	0.01	935,284	99.00	0.000514	0.17	58,410
50.00	0.000051	0.02	584,225	99.50	0.000609	0.20	49,288
60.00	0.000076	0.03	395,223	99.75	0.000720	0.24	41,659
70.00	0.000107	0.04	281,625	99.90	0.000904	0.30	33,194
80.00	0.000148	0.05	202,121				

Ver. 4.02, 05-10-c
DEEM-FCID ACUTE Analysis for DICROTOPHOS NHANES 2005-2010 2-Day
Residue file: Dicrotophos acute water ppb.R10 Adjustment factor #2 NOT used.
Analysis Date: 12-14-2016/08:44:20 Residue file dated: 12-14-2016/08:40:13
NOEL (Acute) = 30.000000 mg/kg body-wt/day
Acute Reference Dose (aRfD) = 0.300000 mg/kg body-wt/day
RAC/FF intake summed over 24 hours
MC iterations = 100; MC list in residue file; MC seed = 1; RNG = MS VB
Run Comment: "Dose in ug/kg/day, Residue in ppb"
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Youth 13-19

	Daily Exposure Analysis (mg/kg body-weight/day) per Capita	per User
Mean	0.000075	0.000083
Standard Deviation	0.000098	0.000100
Margin of Exposure	400,327	361,496
Percent of aRfD	0.02	0.03

Percent of Person-Days that are User-Days = 90.30%

Estimated percentile of user-days falling below calculated exposure in mg/kg body-wt/day with Margin of Exposure (MOE) and Percent of aRfD

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
10.00	0.000005	0.00	>1,000,000	90.00	0.000201	0.07	149,077
20.00	0.000012	0.00	>1,000,000	95.00	0.000277	0.09	108,469
30.00	0.000021	0.01	>1,000,000	97.50	0.000352	0.12	85,239
40.00	0.000035	0.01	864,486	99.00	0.000452	0.15	66,306
50.00	0.000050	0.02	597,528	99.50	0.000541	0.18	55,467
60.00	0.000070	0.02	429,426	99.75	0.000635	0.21	47,280
70.00	0.000096	0.03	311,139	99.90	0.000785	0.26	38,215
80.00	0.000136	0.05	221,309				

Estimated percentile of per-capita days falling below calculated exposure in mg/kg body-wt/day with Margin of Exposure (MOE) and Percent of aRfD

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
10.00	0.000000	0.00	>1,000,000	90.00	0.000192	0.06	156,340
20.00	0.000006	0.00	>1,000,000	95.00	0.000268	0.09	112,035
30.00	0.000014	0.00	>1,000,000	97.50	0.000343	0.11	87,584
40.00	0.000025	0.01	>1,000,000	99.00	0.000440	0.15	68,176
50.00	0.000042	0.01	717,433	99.50	0.000533	0.18	56,262
60.00	0.000061	0.02	494,825	99.75	0.000633	0.21	47,423
70.00	0.000087	0.03	343,148	99.90	0.000754	0.25	39,777
80.00	0.000125	0.04	240,447				

Ver. 4.02, 05-10-c
DEEM-FCID ACUTE Analysis for DICROTOPHOS NHANES 2005-2010 2-Day
Residue file: Dicrotophos acute water ppb.R10 Adjustment factor #2 NOT used.
Analysis Date: 12-14-2016/08:44:20 Residue file dated: 12-14-2016/08:40:13
NOEL (Acute) = 30.000000 mg/kg body-wt/day
Acute Reference Dose (aRfD) = 0.300000 mg/kg body-wt/day
RAC/FF intake summed over 24 hours
MC iterations = 100; MC list in residue file; MC seed = 1; RNG = MS VB
Run Comment: "Dose in ug/kg/day, Residue in ppb"
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Adults 20-49

	Daily Exposure Analysis (mg/kg body-weight/day) per Capita	per User
Mean	0.000105	0.000109
Standard Deviation	0.000113	0.000114
Margin of Exposure	285,065	274,308
Percent of aRfD	0.04	0.04

Percent of Person-Days that are User-Days = 96.23%

Estimated percentile of user-days falling below calculated exposure in mg/kg body-wt/day with Margin of Exposure (MOE) and Percent of aRfD

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
10.00	0.000009	0.00	>1,000,000	90.00	0.000254	0.08	117,904
20.00	0.000019	0.01	>1,000,000	95.00	0.000328	0.11	91,527
30.00	0.000031	0.01	958,912	97.50	0.000409	0.14	73,304
40.00	0.000051	0.02	592,537	99.00	0.000518	0.17	57,906
50.00	0.000076	0.03	396,516	99.50	0.000598	0.20	50,137
60.00	0.000104	0.03	288,930	99.75	0.000684	0.23	43,828
70.00	0.000137	0.05	218,283	99.90	0.000824	0.27	36,389
80.00	0.000181	0.06	165,884				

Estimated percentile of per-capita days falling below calculated exposure in mg/kg body-wt/day with Margin of Exposure (MOE) and Percent of aRfD

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
10.00	0.000006	0.00	>1,000,000	90.00	0.000250	0.08	119,847
20.00	0.000015	0.01	>1,000,000	95.00	0.000324	0.11	92,640
30.00	0.000027	0.01	>1,000,000	97.50	0.000404	0.13	74,190
40.00	0.000045	0.02	660,041	99.00	0.000510	0.17	58,833
50.00	0.000071	0.02	421,503	99.50	0.000597	0.20	50,281
60.00	0.000099	0.03	303,375	99.75	0.000678	0.23	44,260
70.00	0.000133	0.04	226,130	99.90	0.000818	0.27	36,652
80.00	0.000177	0.06	169,581				

Ver. 4.02, 05-10-c
DEEM-FCID ACUTE Analysis for DICROTOPHOS NHANES 2005-2010 2-Day
Residue file: Dicrotophos acute water ppb.R10 Adjustment factor #2 NOT used.
Analysis Date: 12-14-2016/08:44:20 Residue file dated: 12-14-2016/08:40:13
NOEL (Acute) = 30.000000 mg/kg body-wt/day
Acute Reference Dose (aRfD) = 0.300000 mg/kg body-wt/day
RAC/FF intake summed over 24 hours
MC iterations = 100; MC list in residue file; MC seed = 1; RNG = MS VB
Run Comment: "Dose in ug/kg/day, Residue in ppb"
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Adults 50-99

	Daily Exposure Analysis (mg/kg body-weight/day) per Capita	per User
Mean	0.000103	0.000104
Standard Deviation	0.000101	0.000101
Margin of Exposure	292,623	288,245
Percent of aRfD	0.03	0.03

Percent of Person-Days that are User-Days = 98.50%

Estimated percentile of user-days falling below calculated exposure in mg/kg body-wt/day with Margin of Exposure (MOE) and Percent of aRfD

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
10.00	0.000011	0.00	>1,000,000	90.00	0.000228	0.08	131,450
20.00	0.000020	0.01	>1,000,000	95.00	0.000290	0.10	103,488
30.00	0.000034	0.01	874,921	97.50	0.000353	0.12	85,019
40.00	0.000055	0.02	540,742	99.00	0.000460	0.15	65,147
50.00	0.000079	0.03	378,365	99.50	0.000531	0.18	56,444
60.00	0.000103	0.03	290,190	99.75	0.000635	0.21	47,268
70.00	0.000132	0.04	227,345	99.90	0.000749	0.25	40,079
80.00	0.000170	0.06	176,918				

Estimated percentile of per-capita days falling below calculated exposure in mg/kg body-wt/day with Margin of Exposure (MOE) and Percent of aRfD

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
10.00	0.000010	0.00	>1,000,000	90.00	0.000227	0.08	132,116
20.00	0.000019	0.01	>1,000,000	95.00	0.000288	0.10	104,044
30.00	0.000033	0.01	916,121	97.50	0.000352	0.12	85,309
40.00	0.000054	0.02	560,549	99.00	0.000459	0.15	65,356
50.00	0.000078	0.03	387,043	99.50	0.000530	0.18	56,567
60.00	0.000102	0.03	294,500	99.75	0.000633	0.21	47,390
70.00	0.000131	0.04	229,769	99.90	0.000748	0.25	40,125
80.00	0.000168	0.06	178,305				

Ver. 4.02, 05-10-c
DEEM-FCID ACUTE Analysis for DICROTOPHOS NHANES 2005-2010 2-Day
Residue file: Dicrotophos acute water ppb.R10 Adjustment factor #2 NOT used.
Analysis Date: 12-14-2016/08:44:20 Residue file dated: 12-14-2016/08:40:13
NOEL (Acute) = 30.000000 mg/kg body-wt/day
Acute Reference Dose (aRfD) = 0.300000 mg/kg body-wt/day
RAC/FF intake summed over 24 hours
MC iterations = 100; MC list in residue file; MC seed = 1; RNG = MS VB
Run Comment: "Dose in ug/kg/day, Residue in ppb"
==========

Female 13-49

	Daily Exposure Analysis (mg/kg body-weight/day) per Capita	per User
Mean	0.000103	0.000108
Standard Deviation	0.000114	0.000115
Margin of Exposure	290,023	277,217
Percent of aRfD	0.03	0.04

Percent of Person-Days that are User-Days = 95.58%

Estimated percentile of user-days falling below calculated exposure in mg/kg body-wt/day with Margin of Exposure (MOE) and Percent of aRfD

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
10.00	0.000009	0.00	>1,000,000	90.00	0.000257	0.09	116,765
20.00	0.000018	0.01	>1,000,000	95.00	0.000332	0.11	90,347
30.00	0.000030	0.01	984,913	97.50	0.000411	0.14	72,905
40.00	0.000048	0.02	622,687	99.00	0.000506	0.17	59,288
50.00	0.000072	0.02	415,974	99.50	0.000591	0.20	50,777
60.00	0.000100	0.03	300,040	99.75	0.000683	0.23	43,925
70.00	0.000134	0.04	224,020	99.90	0.000809	0.27	37,086
80.00	0.000181	0.06	165,658				

Estimated percentile of per-capita days falling below calculated exposure in mg/kg body-wt/day with Margin of Exposure (MOE) and Percent of aRfD

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
10.00	0.000005	0.00	>1,000,000	90.00	0.000252	0.08	119,228
20.00	0.000014	0.00	>1,000,000	95.00	0.000326	0.11	92,035
30.00	0.000026	0.01	>1,000,000	97.50	0.000405	0.14	74,001
40.00	0.000043	0.01	693,821	99.00	0.000502	0.17	59,802
50.00	0.000066	0.02	455,659	99.50	0.000585	0.19	51,309
60.00	0.000094	0.03	318,718	99.75	0.000674	0.22	44,531
70.00	0.000129	0.04	232,427	99.90	0.000800	0.27	37,520
80.00	0.000176	0.06	170,571				

Ver. 4.02, 05-10-c
DEEM-FCID ACUTE Analysis for DICROTOPHOS NHANES 2005-2010 2-Day
Residue file: Dicrotophos acute water ppb.R10 Adjustment factor #2 NOT used.
Analysis Date: 12-14-2016/08:44:20 Residue file dated: 12-14-2016/08:40:13
NOEL (Acute) = 30.000000 mg/kg body-wt/day
Acute Reference Dose (aRfD) = 0.300000 mg/kg body-wt/day
RAC/FF intake summed over 24 hours
MC iterations = 100; MC list in residue file; MC seed = 1; RNG = MS VB
Run Comment: "Dose in ug/kg/day, Residue in ppb"
==========

Custom demographics 1: Adults, 18+ yrs
Sex: M/F-all/
All Races
Age-Low: 18 yrs High: 99 yrs

	Daily Exposure Analysis (mg/kg body-weight/day) per Capita	per User
Mean	0.000103	0.000106
Standard Deviation	0.000108	0.000108
Margin of Exposure	290,591	281,892
Percent of aRfD	0.03	0.04

Percent of Person-Days that are User-Days = 97.01%

Estimated percentile of user-days falling below calculated exposure in mg/kg body-wt/day with Margin of Exposure (MOE) and Percent of aRfD

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
10.00	0.000010	0.00	>1,000,000	90.00	0.000242	0.08	123,802
20.00	0.000019	0.01	>1,000,000	95.00	0.000311	0.10	96,349
30.00	0.000032	0.01	928,265	97.50	0.000386	0.13	77,627
40.00	0.000052	0.02	576,840	99.00	0.000490	0.16	61,208
50.00	0.000076	0.03	392,525	99.50	0.000579	0.19	51,842
60.00	0.000103	0.03	292,280	99.75	0.000665	0.22	45,121
70.00	0.000134	0.04	224,420	99.90	0.000781	0.26	38,422
80.00	0.000175	0.06	171,673				

Estimated percentile of per-capita days falling below calculated exposure in mg/kg body-wt/day with Margin of Exposure (MOE) and Percent of aRfD

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
10.00	0.000007	0.00	>1,000,000	90.00	0.000239	0.08	125,543
20.00	0.000017	0.01	>1,000,000	95.00	0.000308	0.10	97,286
30.00	0.000029	0.01	>1,000,000	97.50	0.000383	0.13	78,323
40.00	0.000048	0.02	627,693	99.00	0.000487	0.16	61,655
50.00	0.000073	0.02	413,182	99.50	0.000576	0.19	52,109
60.00	0.000099	0.03	302,643	99.75	0.000661	0.22	45,359
70.00	0.000130	0.04	230,022	99.90	0.000776	0.26	38,657
80.00	0.000172	0.06	174,424				

Ver. 4.02, 05-10-c

DEEM-FCID Acute analysis for DICROTOPHOS
Residue file name: H:\MyFiles\DEEM-FCID Files\Dicrotophos\Dicrotophos v4.02 Files\Dicrotophos acute water ppb.R10
Analysis Date 12-14-2016 Residue file dated: 12-14-2016/08:40:13
Reference dose: aRfD = 0.25 mg/kg bw/day NOEL = 25 mg/kg bw/day
Comment: Dose in ug/kg/day, Residue in ppb

RDL indices and parameters for Monte Carlo Analysis:

Index #	Dist Code	Parameter #1	Param #2	Param #3	Comment
1	6	Drinking Water ppb.rdf			

EPA Code	Crop Grp	Food Name	Def Res (ppm)	Adj.Factors #1	#2	RDL Pntr	Comment
8601000000	86A	Water, direct, all sources	0.009000	1.000	1.000	1	residu
Full comment: residue in ppb							
8602000000	86B	Water, indirect, all sources	0.009000	1.000	1.000	1	residu
Full comment: residue in ppb							

Summary of Residue Distribution Files (RDF) listed in H:\MyFiles\DEEM-FCID Files\Dicrotophos\Dicrotophos v4.02 Files\Dicrotophos acute water ppb.R10

RDF #	File Name	N residues w freq's	N residues w/o freq's	N LODs	LOD Value	N Zeros
1	Drinking Water ppb.rdf	0	400	0	0	0

Ver. 4.02, 05-10-c
DEEM-FCID ACUTE Analysis for DICROTOPHOS NHANES 2005-2010 2-Day
Residue file: Dicrotophos acute water ppb.R10 Adjustment factor #2 NOT used.
Analysis Date: 12-14-2016/15:51:10 Residue file dated: 12-14-2016/08:40:13
NOEL (Acute) = 25.000000 mg/kg body-wt/day
Two-Day Average Results Reported
RAC/FF intake summed over 24 hours
MC iterations = 100; MC list in residue file; MC seed = 1; RNG = MS VB
Run Comment: "Dose in ug/kg/day, Residue in ppb"
==========

Summary calculations--per capita:

--- 95th Percentile----			--- 97.5th Percentile----			---99.9th Percentile----		
Exposure	% aRfD	MOE	Exposure	% aRfD	MOE	Exposure	% aRfD	MOE
Total US Population:								
0.000308	0.12	81226	0.000393	0.16	63608	0.001127	0.45	22184
Nursing Infants:								
0.000546	0.22	45770	0.000726	0.29	34442	0.001812	0.72	13795
Non-Nursing Infants:								
0.001247	0.50	20048	0.001442	0.58	17340	0.002356	0.94	10608
Female 13+ PREG:								
0.000306	0.12	81728	0.000367	0.15	68135	0.000607	0.24	41162
All Infants:								
0.001172	0.47	21338	0.001368	0.55	18268	0.002290	0.92	10917
Children 1-2:								
0.000442	0.18	56498	0.000523	0.21	47815	0.001352	0.54	18486
Children 3-5:								
0.000341	0.14	73221	0.000417	0.17	59983	0.000968	0.39	25832
Children 6-12:								
0.000266	0.11	93810	0.000341	0.14	73275	0.000783	0.31	31917
Youth 13-19:								
0.000247	0.10	101100	0.000310	0.12	80695	0.000568	0.23	44012
Adults 20-49:								
0.000303	0.12	82391	0.000372	0.15	67286	0.000695	0.28	35978
Adults 50-99:								
0.000275	0.11	90797	0.000335	0.13	74708	0.000655	0.26	38148
Female 13-49:								
0.000308	0.12	81047	0.000373	0.15	66952	0.000681	0.27	36703
Custom demographics 1: Adults, 18+ yrs:								
0.000291	0.12	85915	0.000355	0.14	70495	0.000684	0.27	36554

Ver. 4.02, 05-10-c
DEEM-FCID ACUTE Analysis for DICROTOPHOS NHANES 2005-2010 2-Day
Residue file: Dicrotophos acute water ppb.R10 Adjustment factor #2 NOT used.
Analysis Date: 12-14-2016/15:51:10 Residue file dated: 12-14-2016/08:40:13
NOEL (Acute) = 25.000000 mg/kg body-wt/day
Two-Day Average Results Reported
RAC/FF intake summed over 24 hours
MC iterations = 100; MC list in residue file; MC seed = 1; RNG = MS VB
Run Comment: "Dose in ug/kg/day, Residue in ppb"
==========

Summary calculations--users:

--- 95th Percentile----			--- 97.5th Percentile----			---99.9th Percentile----		
Exposure	% aRfD	MOE	Exposure	% aRfD	MOE	Exposure	% aRfD	MOE
Total US Population:								
0.000309	0.12	80866	0.000394	0.16	63402	0.001130	0.45	22119
Nursing Infants:								
0.000668	0.27	37429	0.000839	0.34	29795	0.002357	0.94	10608
Non-Nursing Infants:								
0.001250	0.50	20005	0.001445	0.58	17300	0.002384	0.95	10485
Female 13+ PREG:								
0.000308	0.12	81074	0.000368	0.15	68009	0.000607	0.24	41156
All Infants:								
0.001216	0.49	20558	0.001400	0.56	17858	0.002357	0.94	10608
Children 1-2:								
0.000445	0.18	56167	0.000525	0.21	47632	0.001353	0.54	18473
Children 3-5:								
0.000343	0.14	72911	0.000417	0.17	59882	0.000968	0.39	25826
Children 6-12:								
0.000267	0.11	93531	0.000342	0.14	73108	0.000785	0.31	31836
Youth 13-19:								
0.000249	0.10	100374	0.000311	0.12	80470	0.000570	0.23	43863
Adults 20-49:								
0.000305	0.12	81990	0.000372	0.15	67140	0.000696	0.28	35944
Adults 50-99:								
0.000276	0.11	90740	0.000335	0.13	74660	0.000656	0.26	38126
Female 13-49:								
0.000309	0.12	80783	0.000374	0.15	66850	0.000682	0.27	36666
Custom demographics 1: Adults, 18+ yrs:								
0.000292	0.12	85716	0.000355	0.14	70343	0.000685	0.27	36506

Ver. 4.02, 05-10-c
DEEM-FCID ACUTE Analysis for DICROTOPHOS NHANES 2005-2010 2-Day
Residue file: Dicrotophos acute water ppb.R10 Adjustment factor #2 NOT used.
Analysis Date: 12-14-2016/15:51:10 Residue file dated: 12-14-2016/08:40:13
NOEL (Acute) = 25.000000 mg/kg body-wt/day
Acute Reference Dose (aRfD) = 0.250000 mg/kg body-wt/day
Two-Day Average Results Reported
RAC/FF intake summed over 24 hours
MC iterations = 100; MC list in residue file; MC seed = 1; RNG = MS VB
Run Comment: "Dose in ug/kg/day, Residue in ppb"

Total US Population	2-Day Avg Exposure Analysis /a (mg/kg body-weight/day) per Capita	per User
Mean	0.000106	0.000107
Standard Deviation	0.000119	0.000119
Margin of Exposure 2/	235,925	232,971
Percent of aRfD	0.04	0.04

Percent of Individuals that are Users (over two days) = 98.75%

Estimated percentile of user-days falling below calculated exposure in mg/kg body-wt/day with Margin of Exposure (MOE) and Percent of aRfD

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
10.00	0.000010	0.00	>1,000,000	90.00	0.000238	0.10	104,940
20.00	0.000019	0.01	>1,000,000	95.00	0.000309	0.12	80,866
30.00	0.000032	0.01	778,707	97.50	0.000394	0.16	63,402
40.00	0.000053	0.02	473,515	99.00	0.000531	0.21	47,069
50.00	0.000077	0.03	326,522	99.50	0.000681	0.27	36,705
60.00	0.000102	0.04	245,255	99.75	0.000857	0.34	29,186
70.00	0.000132	0.05	189,912	99.90	0.001130	0.45	22,119
80.00	0.000171	0.07	146,249				

Estimated percentile of per-capita days falling below calculated exposure in mg/kg body-wt/day with Margin of Exposure (MOE) and Percent of aRfD

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
10.00	0.000009	0.00	>1,000,000	90.00	0.000237	0.09	105,418
20.00	0.000018	0.01	>1,000,000	95.00	0.000308	0.12	81,226
30.00	0.000031	0.01	814,107	97.50	0.000393	0.16	63,608
40.00	0.000051	0.02	489,698	99.00	0.000528	0.21	47,312
50.00	0.000075	0.03	333,949	99.50	0.000679	0.27	36,823
60.00	0.000101	0.04	248,153	99.75	0.000853	0.34	29,314
70.00	0.000130	0.05	191,607	99.90	0.001127	0.45	22,184
80.00	0.000170	0.07	147,110				

a/ Analysis based on all two-day participant records in NHANES 2005-2010 2-Day with 2 days of valid drinking water records.
2/ Margin of Exposure = NOEL/ Dietary Exposure.

Ver. 4.02, 05-10-c
DEEM-FCID ACUTE Analysis for DICROTOPHOS NHANES 2005-2010 2-Day
Residue file: Dicrotophos acute water ppb.R10 Adjustment factor #2 NOT used.
Analysis Date: 12-14-2016/15:51:10 Residue file dated: 12-14-2016/08:40:13
NOEL (Acute) = 25.000000 mg/kg body-wt/day
Acute Reference Dose (aRfD) = 0.250000 mg/kg body-wt/day
Two-Day Average Results Reported
RAC/FF intake summed over 24 hours
MC iterations = 100; MC list in residue file; MC seed = 1; RNG = MS VB
Run Comment: "Dose in ug/kg/day, Residue in ppb"
==========

Nursing Infants

2-Day Avg Exposure Analysis
(mg/kg body-weight/day)

	per Capita	per User
Mean	0.000120	0.000191
Standard Deviation	0.000224	0.000257
Margin of Exposure	207,838	130,995
Percent of aRfD	0.05	0.08

Percent of Individuals that are Users (over two days) = 63.03%

Estimated percentile of user-days falling below calculated exposure in mg/kg body-wt/day with Margin of Exposure (MOE) and Percent of aRfD

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
10.00	0.000007	0.00	>1,000,000	90.00	0.000523	0.21	47,784
20.00	0.000017	0.01	>1,000,000	95.00	0.000668	0.27	37,429
30.00	0.000034	0.01	731,917	97.50	0.000839	0.34	29,795
40.00	0.000060	0.02	418,326	99.00	0.001077	0.43	23,208
50.00	0.000093	0.04	269,909	99.50	0.001565	0.63	15,977
60.00	0.000143	0.06	174,218	99.75	0.001803	0.72	13,866
70.00	0.000203	0.08	123,280	99.90	0.002357	0.94	10,608
80.00	0.000332	0.13	75,351				

Estimated percentile of per-capita days falling below calculated exposure in mg/kg body-wt/day with Margin of Exposure (MOE) and Percent of aRfD

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
10.00	0.000000	0.00	>1,000,000	90.00	0.000397	0.16	62,914
20.00	0.000000	0.00	>1,000,000	95.00	0.000546	0.22	45,770
30.00	0.000000	0.00	>1,000,000	97.50	0.000726	0.29	34,442
40.00	0.000003	0.00	>1,000,000	99.00	0.000999	0.40	25,028
50.00	0.000018	0.01	>1,000,000	99.50	0.001205	0.48	20,746
60.00	0.000049	0.02	510,382	99.75	0.001576	0.63	15,865
70.00	0.000105	0.04	238,759	99.90	0.001812	0.72	13,795
80.00	0.000188	0.08	132,636				

Ver. 4.02, 05-10-c
DEEM-FCID ACUTE Analysis for DICROTOPHOS NHANES 2005-2010 2-Day
Residue file: Dicrotophos acute water ppb.R10 Adjustment factor #2 NOT used.
Analysis Date: 12-14-2016/15:51:10 Residue file dated: 12-14-2016/08:40:13
NOEL (Acute) = 25.000000 mg/kg body-wt/day
Acute Reference Dose (aRfD) = 0.250000 mg/kg body-wt/day
Two-Day Average Results Reported
RAC/FF intake summed over 24 hours
MC iterations = 100; MC list in residue file; MC seed = 1; RNG = MS VB
Run Comment: "Dose in ug/kg/day, Residue in ppb"
==========

Non-Nursing Infants

2-Day Avg Exposure Analysis
(mg/kg body-weight/day)

	per Capita	per User
Mean	0.000523	0.000531
Standard Deviation	0.000409	0.000407
Margin of Exposure	47,840	47,117
Percent of aRfD	0.21	0.21

Percent of Individuals that are Users (over two days) = 98.49%

Estimated percentile of user-days falling below calculated exposure in mg/kg body-wt/day with Margin of Exposure (MOE) and Percent of aRfD

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
10.00	0.000071	0.03	353,625	90.00	0.001063	0.43	23,520
20.00	0.000107	0.04	233,035	95.00	0.001250	0.50	20,005
30.00	0.000187	0.07	133,458	97.50	0.001445	0.58	17,300
40.00	0.000386	0.15	64,729	99.00	0.001715	0.69	14,576
50.00	0.000507	0.20	49,292	99.50	0.001876	0.75	13,329
60.00	0.000606	0.24	41,249	99.75	0.002082	0.83	12,005
70.00	0.000712	0.28	35,132	99.90	0.002384	0.95	10,485
80.00	0.000847	0.34	29,509				

Estimated percentile of per-capita days falling below calculated exposure in mg/kg body-wt/day with Margin of Exposure (MOE) and Percent of aRfD

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
10.00	0.000065	0.03	383,337	90.00	0.001055	0.42	23,685
20.00	0.000103	0.04	243,768	95.00	0.001247	0.50	20,048
30.00	0.000172	0.07	144,932	97.50	0.001442	0.58	17,340
40.00	0.000372	0.15	67,240	99.00	0.001714	0.69	14,589
50.00	0.000497	0.20	50,319	99.50	0.001874	0.75	13,339
60.00	0.000601	0.24	41,570	99.75	0.002081	0.83	12,011
70.00	0.000708	0.28	35,296	99.90	0.002356	0.94	10,608
80.00	0.000844	0.34	29,622				

Ver. 4.02, 05-10-c
DEEM-FCID ACUTE Analysis for DICROTOPHOS NHANES 2005-2010 2-Day
Residue file: Dicrotophos acute water ppb.R10 Adjustment factor #2 NOT used.
Analysis Date: 12-14-2016/15:51:10 Residue file dated: 12-14-2016/08:40:13
NOEL (Acute) = 25.000000 mg/kg body-wt/day
Acute Reference Dose (aRfD) = 0.250000 mg/kg body-wt/day
Two-Day Average Results Reported
RAC/FF intake summed over 24 hours
MC iterations = 100; MC list in residue file; MC seed = 1; RNG = MS VB
Run Comment: "Dose in ug/kg/day, Residue in ppb"
==========

Female 13+ PREG

2-Day Avg Exposure Analysis
(mg/kg body-weight/day)

	per Capita	per User
Mean	0.000110	0.000112
Standard Deviation	0.000101	0.000101
Margin of Exposure	227,182	223,634
Percent of aRfD	0.04	0.04

Percent of Individuals that are Users (over two days) = 98.44%

Estimated percentile of user-days falling below calculated exposure in mg/kg body-wt/day with Margin of Exposure (MOE) and Percent of aRfD

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
10.00	0.000012	0.00	>1,000,000	90.00	0.000256	0.10	97,601
20.00	0.000023	0.01	>1,000,000	95.00	0.000308	0.12	81,074
30.00	0.000041	0.02	615,063	97.50	0.000368	0.15	68,009
40.00	0.000063	0.03	394,324	99.00	0.000423	0.17	59,032
50.00	0.000085	0.03	295,063	99.50	0.000479	0.19	52,177
60.00	0.000109	0.04	228,815	99.75	0.000564	0.23	44,299
70.00	0.000141	0.06	176,735	99.90	0.000607	0.24	41,156
80.00	0.000189	0.08	132,078				

Estimated percentile of per-capita days falling below calculated exposure in mg/kg body-wt/day with Margin of Exposure (MOE) and Percent of aRfD

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
10.00	0.000010	0.00	>1,000,000	90.00	0.000255	0.10	97,858
20.00	0.000021	0.01	>1,000,000	95.00	0.000306	0.12	81,728
30.00	0.000038	0.02	651,627	97.50	0.000367	0.15	68,135
40.00	0.000062	0.02	405,503	99.00	0.000423	0.17	59,161
50.00	0.000084	0.03	298,269	99.50	0.000479	0.19	52,193
60.00	0.000106	0.04	234,836	99.75	0.000564	0.23	44,352
70.00	0.000141	0.06	177,811	99.90	0.000607	0.24	41,162
80.00	0.000188	0.08	132,670				

Ver. 4.02, 05-10-c
DEEM-FCID ACUTE Analysis for DICROTOPHOS NHANES 2005-2010 2-Day
Residue file: Dicrotophos acute water ppb.R10 Adjustment factor #2 NOT used.
Analysis Date: 12-14-2016/15:51:10 Residue file dated: 12-14-2016/08:40:13
NOEL (Acute) = 25.000000 mg/kg body-wt/day
Acute Reference Dose (aRfD) = 0.250000 mg/kg body-wt/day
Two-Day Average Results Reported
RAC/FF intake summed over 24 hours
MC iterations = 100; MC list in residue file; MC seed = 1; RNG = MS VB
Run Comment: "Dose in ug/kg/day, Residue in ppb"
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All Infants

2-Day Avg Exposure Analysis
(mg/kg body-weight/day)

	per Capita	per User
Mean	0.000396	0.000453
Standard Deviation	0.000407	0.000404
Margin of Exposure	63,125	55,130
Percent of aRfD	0.16	0.18

Percent of Individuals that are Users (over two days) = 87.33%

Estimated percentile of user-days falling below calculated exposure in mg/kg body-wt/day with Margin of Exposure (MOE) and Percent of aRfD

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
10.00	0.000038	0.02	661,016	90.00	0.001002	0.40	24,956
20.00	0.000080	0.03	310,608	95.00	0.001216	0.49	20,558
30.00	0.000122	0.05	205,137	97.50	0.001400	0.56	17,858
40.00	0.000204	0.08	122,304	99.00	0.001693	0.68	14,766
50.00	0.000388	0.16	64,355	99.50	0.001843	0.74	13,566
60.00	0.000522	0.21	47,938	99.75	0.002062	0.82	12,124
70.00	0.000639	0.26	39,127	99.90	0.002357	0.94	10,608
80.00	0.000787	0.31	31,772				

Estimated percentile of per-capita days falling below calculated exposure in mg/kg body-wt/day with Margin of Exposure (MOE) and Percent of aRfD

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
10.00	0.000000	0.00	>1,000,000	90.00	0.000956	0.38	26,155
20.00	0.000029	0.01	858,721	95.00	0.001172	0.47	21,338
30.00	0.000080	0.03	313,392	97.50	0.001368	0.55	18,268
40.00	0.000127	0.05	197,165	99.00	0.001616	0.65	15,468
50.00	0.000257	0.10	97,200	99.50	0.001822	0.73	13,719
60.00	0.000444	0.18	56,261	99.75	0.002007	0.80	12,457
70.00	0.000589	0.24	42,440	99.90	0.002290	0.92	10,917
80.00	0.000733	0.29	34,094				

Ver. 4.02, 05-10-c
DEEM-FCID ACUTE Analysis for DICROTOPHOS NHANES 2005-2010 2-Day
Residue file: Dicrotophos acute water ppb.R10 Adjustment factor #2 NOT used.
Analysis Date: 12-14-2016/15:51:10 Residue file dated: 12-14-2016/08:40:13
NOEL (Acute) = 25.000000 mg/kg body-wt/day
Acute Reference Dose (aRfD) = 0.250000 mg/kg body-wt/day
Two-Day Average Results Reported
RAC/FF intake summed over 24 hours
MC iterations = 100; MC list in residue file; MC seed = 1; RNG = MS VB
Run Comment: "Dose in ug/kg/day, Residue in ppb"
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Children 1-2

	2-Day Avg Exposure Analysis (mg/kg body-weight/day) per Capita	per User
Mean	0.000146	0.000148
Standard Deviation	0.000156	0.000157
Margin of Exposure	171,777	168,939
Percent of aRfD	0.06	0.06

Percent of Individuals that are Users (over two days) = 98.35%

Estimated percentile of user-days falling below calculated exposure in mg/kg body-wt/day with Margin of Exposure (MOE) and Percent of aRfD

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
10.00	0.000014	0.01	>1,000,000	90.00	0.000347	0.14	72,107
20.00	0.000026	0.01	979,196	95.00	0.000445	0.18	56,167
30.00	0.000043	0.02	578,138	97.50	0.000525	0.21	47,632
40.00	0.000071	0.03	354,344	99.00	0.000667	0.27	37,472
50.00	0.000105	0.04	237,261	99.50	0.000769	0.31	32,503
60.00	0.000139	0.06	179,778	99.75	0.000875	0.35	28,574
70.00	0.000180	0.07	139,153	99.90	0.001353	0.54	18,473
80.00	0.000244	0.10	102,378				

Estimated percentile of per-capita days falling below calculated exposure in mg/kg body-wt/day with Margin of Exposure (MOE) and Percent of aRfD

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
10.00	0.000012	0.00	>1,000,000	90.00	0.000345	0.14	72,394
20.00	0.000024	0.01	>1,000,000	95.00	0.000442	0.18	56,498
30.00	0.000042	0.02	599,496	97.50	0.000523	0.21	47,815
40.00	0.000068	0.03	367,826	99.00	0.000665	0.27	37,614
50.00	0.000102	0.04	244,939	99.50	0.000768	0.31	32,549
60.00	0.000137	0.05	182,170	99.75	0.000873	0.35	28,638
70.00	0.000177	0.07	141,277	99.90	0.001352	0.54	18,486
80.00	0.000242	0.10	103,349				

Residue file: Dicrotophos acute water ppb.R10 Adjustment factor #2 NOT used.
Analysis Date: 12-14-2016/15:51:10 Residue file dated: 12-14-2016/08:40:13
NOEL (Acute) = 25.000000 mg/kg body-wt/day
Acute Reference Dose (aRfD) = 0.250000 mg/kg body-wt/day
Two-Day Average Results Reported
RAC/FF intake summed over 24 hours
MC iterations = 100; MC list in residue file; MC seed = 1; RNG = MS VB
Run Comment: "Dose in ug/kg/day, Residue in ppb"
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Children 3-5

2-Day Avg Exposure Analysis
(mg/kg body-weight/day)

	per Capita	per User
Mean	0.000119	0.000120
Standard Deviation	0.000121	0.000121
Margin of Exposure	209,343	207,826
Percent of aRfD	0.05	0.05

Percent of Individuals that are Users (over two days) = 99.28%

Estimated percentile of user-days falling below calculated exposure in mg/kg body-wt/day with Margin of Exposure (MOE) and Percent of aRfD

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
10.00	0.000011	0.00	>1,000,000	90.00	0.000272	0.11	91,846
20.00	0.000022	0.01	>1,000,000	95.00	0.000343	0.14	72,911
30.00	0.000036	0.01	689,517	97.50	0.000417	0.17	59,882
40.00	0.000058	0.02	430,990	99.00	0.000549	0.22	45,513
50.00	0.000085	0.03	293,045	99.50	0.000659	0.26	37,942
60.00	0.000117	0.05	214,584	99.75	0.000759	0.30	32,943
70.00	0.000154	0.06	162,017	99.90	0.000968	0.39	25,826
80.00	0.000201	0.08	124,298				

Estimated percentile of per-capita days falling below calculated exposure in mg/kg body-wt/day with Margin of Exposure (MOE) and Percent of aRfD

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
10.00	0.000011	0.00	>1,000,000	90.00	0.000271	0.11	92,131
20.00	0.000022	0.01	>1,000,000	95.00	0.000341	0.14	73,221
30.00	0.000035	0.01	713,624	97.50	0.000417	0.17	59,983
40.00	0.000057	0.02	439,014	99.00	0.000548	0.22	45,581
50.00	0.000085	0.03	294,874	99.50	0.000654	0.26	38,216
60.00	0.000116	0.05	216,337	99.75	0.000759	0.30	32,956
70.00	0.000153	0.06	163,684	99.90	0.000968	0.39	25,832
80.00	0.000201	0.08	124,644				

Ver. 4.02, 05-10-c
DEEM-FCID ACUTE Analysis for DICROTOPHOS NHANES 2005-2010 2-Day
Residue file: Dicrotophos acute water ppb.R10 Adjustment factor #2 NOT used.
Analysis Date: 12-14-2016/15:51:10 Residue file dated: 12-14-2016/08:40:13
NOEL (Acute) = 25.000000 mg/kg body-wt/day
Acute Reference Dose (aRfD) = 0.250000 mg/kg body-wt/day
Two-Day Average Results Reported
RAC/FF intake summed over 24 hours
MC iterations = 100; MC list in residue file; MC seed = 1; RNG = MS VB
Run Comment: "Dose in ug/kg/day, Residue in ppb"
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Children 6-12

2-Day Avg Exposure Analysis
(mg/kg body-weight/day)

	per Capita	per User
Mean	0.000088	0.000090
Standard Deviation	0.000096	0.000097
Margin of Exposure	283,936	278,810
Percent of aRfD	0.04	0.04

Percent of Individuals that are Users (over two days) = 98.19%

Estimated percentile of user-days falling below calculated exposure in mg/kg body-wt/day with Margin of Exposure (MOE) and Percent of aRfD

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
10.00	0.000008	0.00	>1,000,000	90.00	0.000203	0.08	123,362
20.00	0.000016	0.01	>1,000,000	95.00	0.000267	0.11	93,531
30.00	0.000026	0.01	968,194	97.50	0.000342	0.14	73,108
40.00	0.000043	0.02	584,731	99.00	0.000432	0.17	57,833
50.00	0.000063	0.03	397,436	99.50	0.000523	0.21	47,761
60.00	0.000083	0.03	300,402	99.75	0.000640	0.26	39,032
70.00	0.000111	0.04	226,042	99.90	0.000785	0.31	31,836
80.00	0.000146	0.06	170,991				

Estimated percentile of per-capita days falling below calculated exposure in mg/kg body-wt/day with Margin of Exposure (MOE) and Percent of aRfD

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
10.00	0.000007	0.00	>1,000,000	90.00	0.000201	0.08	124,238
20.00	0.000014	0.01	>1,000,000	95.00	0.000266	0.11	93,810
30.00	0.000024	0.01	>1,000,000	97.50	0.000341	0.14	73,275
40.00	0.000040	0.02	622,768	99.00	0.000430	0.17	58,138
50.00	0.000061	0.02	409,078	99.50	0.000522	0.21	47,932
60.00	0.000082	0.03	306,138	99.75	0.000640	0.26	39,086
70.00	0.000109	0.04	230,081	99.90	0.000783	0.31	31,917
80.00	0.000145	0.06	172,170				

Ver. 4.02, 05-10-c
DEEM-FCID ACUTE Analysis for DICROTOPHOS NHANES 2005-2010 2-Day
Residue file: Dicrotophos acute water ppb.R10 Adjustment factor #2 NOT used.
Analysis Date: 12-14-2016/15:51:10 Residue file dated: 12-14-2016/08:40:13
NOEL (Acute) = 25.000000 mg/kg body-wt/day
Acute Reference Dose (aRfD) = 0.250000 mg/kg body-wt/day
Two-Day Average Results Reported
RAC/FF intake summed over 24 hours
MC iterations = 100; MC list in residue file; MC seed = 1; RNG = MS VB
Run Comment: "Dose in ug/kg/day, Residue in ppb"
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Youth 13-19

2-Day Avg Exposure Analysis
(mg/kg body-weight/day)

	per Capita	per User
Mean	0.000075	0.000077
Standard Deviation	0.000085	0.000085
Margin of Exposure	335,296	324,781
Percent of aRfD	0.03	0.03

Percent of Individuals that are Users (over two days) = 96.86%

Estimated percentile of user-days falling below calculated exposure in mg/kg body-wt/day with Margin of Exposure (MOE) and Percent of aRfD

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
10.00	0.000006	0.00	>1,000,000	90.00	0.000184	0.07	135,923
20.00	0.000012	0.00	>1,000,000	95.00	0.000249	0.10	100,374
30.00	0.000021	0.01	>1,000,000	97.50	0.000311	0.12	80,470
40.00	0.000033	0.01	750,620	99.00	0.000375	0.15	66,697
50.00	0.000050	0.02	500,259	99.50	0.000453	0.18	55,147
60.00	0.000068	0.03	365,724	99.75	0.000530	0.21	47,129
70.00	0.000094	0.04	265,768	99.90	0.000570	0.23	43,863
80.00	0.000124	0.05	200,918				

Estimated percentile of per-capita days falling below calculated exposure in mg/kg body-wt/day with Margin of Exposure (MOE) and Percent of aRfD

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
10.00	0.000004	0.00	>1,000,000	90.00	0.000180	0.07	138,619
20.00	0.000010	0.00	>1,000,000	95.00	0.000247	0.10	101,100
30.00	0.000018	0.01	>1,000,000	97.50	0.000310	0.12	80,695
40.00	0.000031	0.01	814,125	99.00	0.000374	0.15	66,764
50.00	0.000047	0.02	534,535	99.50	0.000451	0.18	55,375
60.00	0.000066	0.03	381,426	99.75	0.000529	0.21	47,292
70.00	0.000091	0.04	273,409	99.90	0.000568	0.23	44,012
80.00	0.000122	0.05	205,335				

Ver. 4.02, 05-10-c
DEEM-FCID ACUTE Analysis for DICROTOPHOS NHANES 2005-2010 2-Day
Residue file: Dicrotophos acute water ppb.R10 Adjustment factor #2 NOT used.
Analysis Date: 12-14-2016/15:51:10 Residue file dated: 12-14-2016/08:40:13
NOEL (Acute) = 25.000000 mg/kg body-wt/day
Acute Reference Dose (aRfD) = 0.250000 mg/kg body-wt/day
Two-Day Average Results Reported
RAC/FF intake summed over 24 hours
MC iterations = 100; MC list in residue file; MC seed = 1; RNG = MS VB
Run Comment: "Dose in ug/kg/day, Residue in ppb"
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Adults 20-49

	2-Day Avg Exposure Analysis (mg/kg body-weight/day) per Capita	per User
Mean	0.000105	0.000106
Standard Deviation	0.000104	0.000104
Margin of Exposure	237,339	235,057
Percent of aRfD	0.04	0.04

Percent of Individuals that are Users (over two days) = 99.04%

Estimated percentile of user-days falling below calculated exposure in mg/kg body-wt/day with Margin of Exposure (MOE) and Percent of aRfD

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
10.00	0.000010	0.00	>1,000,000	90.00	0.000244	0.10	102,582
20.00	0.000019	0.01	>1,000,000	95.00	0.000305	0.12	81,990
30.00	0.000033	0.01	759,037	97.50	0.000372	0.15	67,140
40.00	0.000053	0.02	468,540	99.00	0.000461	0.18	54,196
50.00	0.000079	0.03	317,185	99.50	0.000523	0.21	47,788
60.00	0.000105	0.04	237,441	99.75	0.000596	0.24	41,981
70.00	0.000136	0.05	184,147	99.90	0.000696	0.28	35,944
80.00	0.000176	0.07	141,793				

Estimated percentile of per-capita days falling below calculated exposure in mg/kg body-wt/day with Margin of Exposure (MOE) and Percent of aRfD

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
10.00	0.000010	0.00	>1,000,000	90.00	0.000243	0.10	102,920
20.00	0.000019	0.01	>1,000,000	95.00	0.000303	0.12	82,391
30.00	0.000032	0.01	786,770	97.50	0.000372	0.15	67,286
40.00	0.000052	0.02	480,392	99.00	0.000460	0.18	54,339
50.00	0.000077	0.03	323,236	99.50	0.000523	0.21	47,846
60.00	0.000104	0.04	239,871	99.75	0.000595	0.24	42,051
70.00	0.000135	0.05	185,518	99.90	0.000695	0.28	35,978
80.00	0.000175	0.07	142,578				

Ver. 4.02, 05-10-c
DEEM-FCID ACUTE Analysis for DICROTOPHOS NHANES 2005-2010 2-Day
Residue file: Dicrotophos acute water ppb.R10 Adjustment factor #2 NOT used.
Analysis Date: 12-14-2016/15:51:10 Residue file dated: 12-14-2016/08:40:13
NOEL (Acute) = 25.000000 mg/kg body-wt/day
Acute Reference Dose (aRfD) = 0.250000 mg/kg body-wt/day
Two-Day Average Results Reported
RAC/FF intake summed over 24 hours
MC iterations = 100; MC list in residue file; MC seed = 1; RNG = MS VB
Run Comment: "Dose in ug/kg/day, Residue in ppb"
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Adults 50-99

	2-Day Avg Exposure Analysis (mg/kg body-weight/day) per Capita	per User
Mean	0.000102	0.000103
Standard Deviation	0.000093	0.000093
Margin of Exposure	244,389	243,603
Percent of aRfD	0.04	0.04

Percent of Individuals that are Users (over two days) = 99.68%

Estimated percentile of user-days falling below calculated exposure in mg/kg body-wt/day with Margin of Exposure (MOE) and Percent of aRfD

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
10.00	0.000012	0.00	>1,000,000	90.00	0.000219	0.09	113,943
20.00	0.000021	0.01	>1,000,000	95.00	0.000276	0.11	90,740
30.00	0.000036	0.01	698,985	97.50	0.000335	0.13	74,660
40.00	0.000060	0.02	419,766	99.00	0.000415	0.17	60,203
50.00	0.000083	0.03	301,307	99.50	0.000484	0.19	51,615
60.00	0.000106	0.04	235,380	99.75	0.000559	0.22	44,703
70.00	0.000133	0.05	188,334	99.90	0.000656	0.26	38,126
80.00	0.000166	0.07	150,182				

Estimated percentile of per-capita days falling below calculated exposure in mg/kg body-wt/day with Margin of Exposure (MOE) and Percent of aRfD

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
10.00	0.000012	0.00	>1,000,000	90.00	0.000219	0.09	114,090
20.00	0.000020	0.01	>1,000,000	95.00	0.000275	0.11	90,797
30.00	0.000035	0.01	709,078	97.50	0.000335	0.13	74,708
40.00	0.000059	0.02	422,342	99.00	0.000415	0.17	60,229
50.00	0.000083	0.03	302,585	99.50	0.000484	0.19	51,625
60.00	0.000106	0.04	235,977	99.75	0.000558	0.22	44,769
70.00	0.000132	0.05	188,759	99.90	0.000655	0.26	38,148
80.00	0.000166	0.07	150,380				

Residue file: Dicrotophos acute water ppb.R10 Adjustment factor #2 NOT used.
Analysis Date: 12-14-2016/15:51:10 Residue file dated: 12-14-2016/08:40:13
NOEL (Acute) = 25.000000 mg/kg body-wt/day
Acute Reference Dose (aRfD) = 0.250000 mg/kg body-wt/day
Two-Day Average Results Reported
RAC/FF intake summed over 24 hours
MC iterations = 100; MC list in residue file; MC seed = 1; RNG = MS VB
Run Comment: "Dose in ug/kg/day, Residue in ppb"
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Female 13-49

2-Day Avg Exposure Analysis
(mg/kg body-weight/day)

	per Capita	per User
Mean	0.000103	0.000105
Standard Deviation	0.000105	0.000105
Margin of Exposure	241,759	238,696
Percent of aRfD	0.04	0.04

Percent of Individuals that are Users (over two days) = 98.73%

Estimated percentile of user-days falling below calculated exposure in mg/kg body-wt/day with Margin of Exposure (MOE) and Percent of aRfD

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
10.00	0.000010	0.00	>1,000,000	90.00	0.000249	0.10	100,324
20.00	0.000019	0.01	>1,000,000	95.00	0.000309	0.12	80,783
30.00	0.000032	0.01	784,826	97.50	0.000374	0.15	66,850
40.00	0.000049	0.02	506,517	99.00	0.000458	0.18	54,583
50.00	0.000073	0.03	341,748	99.50	0.000521	0.21	47,952
60.00	0.000100	0.04	250,645	99.75	0.000590	0.24	42,387
70.00	0.000132	0.05	189,649	99.90	0.000682	0.27	36,666
80.00	0.000175	0.07	142,504				

Estimated percentile of per-capita days falling below calculated exposure in mg/kg body-wt/day with Margin of Exposure (MOE) and Percent of aRfD

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
10.00	0.000009	0.00	>1,000,000	90.00	0.000248	0.10	100,949
20.00	0.000018	0.01	>1,000,000	95.00	0.000308	0.12	81,047
30.00	0.000030	0.01	820,319	97.50	0.000373	0.15	66,952
40.00	0.000048	0.02	525,593	99.00	0.000457	0.18	54,677
50.00	0.000071	0.03	350,813	99.50	0.000521	0.21	48,018
60.00	0.000098	0.04	254,586	99.75	0.000589	0.24	42,435
70.00	0.000130	0.05	191,905	99.90	0.000681	0.27	36,703
80.00	0.000174	0.07	143,671				

DEEM-FCID ACUTE Analysis for DICROTOPHOS NHANES 2005-2010 2-Day
Residue file: Dicrotophos acute water ppb.R10 Adjustment factor #2 NOT used.
Analysis Date: 12-14-2016/15:51:10 Residue file dated: 12-14-2016/08:40:13
NOEL (Acute) = 25.000000 mg/kg body-wt/day
Acute Reference Dose (aRfD) = 0.250000 mg/kg body-wt/day
Two-Day Average Results Reported
RAC/FF intake summed over 24 hours
MC iterations = 100; MC list in residue file; MC seed = 1; RNG = MS VB
Run Comment: "Dose in ug/kg/day, Residue in ppb"
==========

Custom demographics 1: Adults, 18+ yrs
Sex: M/F-all/
All Races
Age-Low: 18 yrs High: 99 yrs

	2-Day Avg Exposure Analysis (mg/kg body-weight/day) per Capita	per User
Mean	0.000103	0.000104
Standard Deviation	0.000099	0.000099
Margin of Exposure	242,288	240,461
Percent of aRfD	0.04	0.04

Percent of Individuals that are Users (over two days) = 99.25%

Estimated percentile of user-days falling below calculated exposure in mg/kg body-wt/day with Margin of Exposure (MOE) and Percent of aRfD

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
10.00	0.000011	0.00	>1,000,000	90.00	0.000233	0.09	107,211
20.00	0.000020	0.01	>1,000,000	95.00	0.000292	0.12	85,716
30.00	0.000033	0.01	748,196	97.50	0.000355	0.14	70,343
40.00	0.000055	0.02	452,502	99.00	0.000442	0.18	56,560
50.00	0.000080	0.03	313,792	99.50	0.000508	0.20	49,167
60.00	0.000105	0.04	238,901	99.75	0.000581	0.23	43,059
70.00	0.000133	0.05	187,744	99.90	0.000685	0.27	36,506
80.00	0.000171	0.07	146,559				

Estimated percentile of per-capita days falling below calculated exposure in mg/kg body-wt/day with Margin of Exposure (MOE) and Percent of aRfD

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
10.00	0.000010	0.00	>1,000,000	90.00	0.000232	0.09	107,554
20.00	0.000019	0.01	>1,000,000	95.00	0.000291	0.12	85,915
30.00	0.000033	0.01	769,087	97.50	0.000355	0.14	70,495
40.00	0.000054	0.02	461,815	99.00	0.000441	0.18	56,658
50.00	0.000079	0.03	317,606	99.50	0.000508	0.20	49,226
60.00	0.000104	0.04	240,750	99.75	0.000580	0.23	43,085
70.00	0.000132	0.05	188,716	99.90	0.000684	0.27	36,554
80.00	0.000170	0.07	147,032				

Ver. 4.02, 05-10-c

DEEM-FCID Acute analysis for DICROTOPHOS
Residue file name: H:\MyFiles\DEEM-FCID Files\Dicrotophos\Dicrotophos v4.02 Files\Dicrotophos acute food+water ppb.R10
Analysis Date 12-14-2016 Residue file dated: 12-14-2016/09:05:28
Reference dose: aRfD = 0.3 mg/kg bw/day NOEL = 30 mg/kg bw/day
Comment: Dose in ug/kg/day, Residue in ppb

RDL indices and parameters for Monte Carlo Analysis:

Index #	Dist Code	Parameter #1	Param #2	Param #3	Comment
1	6	Drinking Water ppb.rdf			

EPA Code	Crop Grp	Food Name	Def Res (ppm)	Adj.Factors #1	#2	RDL Pntr	Comment
2003128000	20C	Cottonseed, oil	40.000000	1.000	1.000		residu
Full comment: residue in ppb							
2003128001	20C	Cottonseed, oil-babyfood	40.000000	1.000	1.000		residu
Full comment: residue in ppb							
8601000000	86A	Water, direct, all sources	0.009000	1.000	1.000	1	residu
Full comment: residue in ppb							
8602000000	86B	Water, indirect, all sources	0.009000	1.000	1.000	1	residu
Full comment: residue in ppb							

Summary of Residue Distribution Files (RDF) listed in H:\MyFiles\DEEM-FCID Files\Dicrotophos\Dicrotophos v4.02 Files\Dicrotophos acute food+water ppb.R10

RDF #	File Name	N residues w freq's	N residues w/o freq's	N LODs	LOD Value	N Zeros
1	Drinking Water ppb.rdf	0	400	0	0	0

Ver. 4.02, 05-10-c
DEEM-FCID ACUTE Analysis for DICROTOPHOS NHANES 2005-2010 2-Day
Residue file: Dicrotophos acute food+water ppb.R10
Adjustment factor #2 NOT used.
Analysis Date: 12-14-2016/09:36:58 Residue file dated: 12-14-2016/09:05:28
NOEL (Acute) = 30.000000 mg/kg body-wt/day
RAC/FF intake summed over 24 hours
MC iterations = 100; MC list in residue file; MC seed = 1; RNG = MS VB
Run Comment: "Dose in ug/kg/day, Residue in ppb"
==========

Summary calculations--per capita:

--- 95th Percentile----			--- 97.5th Percentile----			---99.9th Percentile----		
Exposure	% aRfD	MOE	Exposure	% aRfD	MOE	Exposure	% aRfD	MOE
Total US Population:								
0.003254	1.08	9219	0.004507	1.50	6657	0.023041	7.68	1301
Nursing Infants:								
0.001077	0.36	27844	0.002313	0.77	12967	0.007122	2.37	4212
Non-Nursing Infants:								
0.002386	0.80	12571	0.003481	1.16	8618	0.011290	3.76	2657
Female 13+ PREG:								
0.002432	0.81	12334	0.003192	1.06	9399	0.004784	1.59	6271
All Infants:								
0.002177	0.73	13780	0.003161	1.05	9491	0.011301	3.77	2654
Children 1-2:								
0.007032	2.34	4266	0.009115	3.04	3291	0.058689	19.56	511
Children 3-5:								
0.006707	2.24	4473	0.008755	2.92	3426	0.063937	21.31	469
Children 6-12:								
0.005282	1.76	5679	0.006953	2.32	4314	0.042376	14.13	707
Youth 13-19:								
0.003384	1.13	8866	0.004732	1.58	6340	0.021335	7.11	1406
Adults 20-49:								
0.002369	0.79	12664	0.003103	1.03	9667	0.020638	6.88	1453
Adults 50-99:								
0.001892	0.63	15860	0.002464	0.82	12174	0.008241	2.75	3640
Female 13-49:								
0.002342	0.78	12809	0.003222	1.07	9310	0.014240	4.75	2106
Custom demographics 1: Adults, 18+ yrs:								
0.002215	0.74	13541	0.002911	0.97	10304	0.016995	5.67	1765

Ver. 4.02, 05-10-c
DEEM-FCID ACUTE Analysis for DICROTOPHOS NHANES 2005-2010 2-Day
Residue file: Dicrotophos acute food+water ppb.R10
Adjustment factor #2 NOT used.
Analysis Date: 12-14-2016/09:36:58 Residue file dated: 12-14-2016/09:05:28
NOEL (Acute) = 30.000000 mg/kg body-wt/day
RAC/FF intake summed over 24 hours
MC iterations = 100; MC list in residue file; MC seed = 1; RNG = MS VB
Run Comment: "Dose in ug/kg/day, Residue in ppb"
==========

Summary calculations--users:

--- 95th Percentile----			--- 97.5th Percentile----			---99.9th Percentile----		
Exposure	% aRfD	MOE	Exposure	% aRfD	MOE	Exposure	% aRfD	MOE
Total US Population:								
0.003260	1.09	9203	0.004513	1.50	6647	0.023055	7.68	1301
Nursing Infants:								
0.001895	0.63	15833	0.003050	1.02	9837	0.007228	2.41	4150
Non-Nursing Infants:								
0.002399	0.80	12503	0.003504	1.17	8561	0.011293	3.76	2656
Female 13+ PREG:								
0.002432	0.81	12334	0.003192	1.06	9399	0.004784	1.59	6271
All Infants:								
0.002352	0.78	12756	0.003375	1.13	8888	0.011326	3.78	2648
Children 1-2:								
0.007043	2.35	4259	0.009127	3.04	3286	0.058694	19.56	511
Children 3-5:								
0.006708	2.24	4471	0.008764	2.92	3422	0.063939	21.31	469
Children 6-12:								
0.005284	1.76	5677	0.006954	2.32	4314	0.042377	14.13	707
Youth 13-19:								
0.003387	1.13	8858	0.004735	1.58	6335	0.021337	7.11	1406
Adults 20-49:								
0.002370	0.79	12660	0.003104	1.03	9664	0.020639	6.88	1453
Adults 50-99:								
0.001892	0.63	15855	0.002465	0.82	12171	0.008242	2.75	3639
Female 13-49:								
0.002343	0.78	12804	0.003223	1.07	9308	0.014243	4.75	2106
Custom demographics 1: Adults, 18+ yrs:								
0.002216	0.74	13537	0.002912	0.97	10302	0.016997	5.67	1765

Ver. 4.02, 05-10-c
DEEM-FCID ACUTE Analysis for DICROTOPHOS NHANES 2005-2010 2-Day
Residue file: Dicrotophos acute food+water ppb.R10
Adjustment factor #2 NOT used.
Analysis Date: 12-14-2016/09:36:58 Residue file dated: 12-14-2016/09:05:28
NOEL (Acute) = 30.000000 mg/kg body-wt/day
Acute Reference Dose (aRfD) = 0.300000 mg/kg body-wt/day
RAC/FF intake summed over 24 hours
MC iterations = 100; MC list in residue file; MC seed = 1; RNG = MS VB
Run Comment: "Dose in ug/kg/day, Residue in ppb"

Total US Population	Daily Exposure Analysis /a (mg/kg body-weight/day) per Capita	per User
Mean	0.001130	0.001134
Standard Deviation	0.001903	0.001905
Margin of Exposure 2/	26,545	26,458
Percent of aRfD	0.38	0.38

Percent of Person-Days that are User-Days = 99.67%

Estimated percentile of user-days falling below calculated exposure in mg/kg body-wt/day with Margin of Exposure (MOE) and Percent of aRfD

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
10.00	0.000177	0.06	169,836	90.00	0.002297	0.77	13,061
20.00	0.000299	0.10	100,458	95.00	0.003260	1.09	9,203
30.00	0.000426	0.14	70,504	97.50	0.004513	1.50	6,647
40.00	0.000567	0.19	52,864	99.00	0.006620	2.21	4,531
50.00	0.000723	0.24	41,487	99.50	0.009457	3.15	3,172
60.00	0.000913	0.30	32,870	99.75	0.015341	5.11	1,955
70.00	0.001168	0.39	25,682	99.90	0.023055	7.68	1,301
80.00	0.001550	0.52	19,357				

Estimated percentile of per-capita days falling below calculated exposure in mg/kg body-wt/day with Margin of Exposure (MOE) and Percent of aRfD

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
10.00	0.000173	0.06	173,354	90.00	0.002292	0.76	13,090
20.00	0.000296	0.10	101,514	95.00	0.003254	1.08	9,219
30.00	0.000423	0.14	70,985	97.50	0.004507	1.50	6,657
40.00	0.000564	0.19	53,153	99.00	0.006611	2.20	4,537
50.00	0.000721	0.24	41,637	99.50	0.009440	3.15	3,177
60.00	0.000910	0.30	32,978	99.75	0.015255	5.09	1,966
70.00	0.001165	0.39	25,748	99.90	0.023041	7.68	1,301
80.00	0.001546	0.52	19,398				

a/ Analysis based on all two-day participant records in NHANES 2005-2010 2-Day with 2 days of valid drinking water records.
2/ Margin of Exposure = NOEL/ Dietary Exposure.

Residue file: Dicrotophos acute food+water ppb.R10
Adjustment factor #2 NOT used.
Analysis Date: 12-14-2016/09:36:58 Residue file dated: 12-14-2016/09:05:28
NOEL (Acute) = 30.000000 mg/kg body-wt/day
Acute Reference Dose (aRfD) = 0.300000 mg/kg body-wt/day
RAC/FF intake summed over 24 hours
MC iterations = 100; MC list in residue file; MC seed = 1; RNG = MS VB
Run Comment: "Dose in ug/kg/day, Residue in ppb"
==========

Nursing Infants

	Daily Exposure Analysis (mg/kg body-weight/day) per Capita	per User
Mean	0.000279	0.000463
Standard Deviation	0.000673	0.000817
Margin of Exposure	107,656	64,820
Percent of aRfD	0.09	0.15

Percent of Person-Days that are User-Days = 60.21%

Estimated percentile of user-days falling below calculated exposure in mg/kg body-wt/day with Margin of Exposure (MOE) and Percent of aRfD

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
10.00	0.000018	0.01	>1,000,000	90.00	0.000927	0.31	32,369
20.00	0.000046	0.02	652,844	95.00	0.001895	0.63	15,833
30.00	0.000089	0.03	338,597	97.50	0.003050	1.02	9,837
40.00	0.000136	0.05	220,705	99.00	0.004296	1.43	6,982
50.00	0.000200	0.07	150,192	99.50	0.004517	1.51	6,641
60.00	0.000340	0.11	88,309	99.75	0.006849	2.28	4,379
70.00	0.000452	0.15	66,341	99.90	0.007228	2.41	4,150
80.00	0.000609	0.20	49,252				

Estimated percentile of per-capita days falling below calculated exposure in mg/kg body-wt/day with Margin of Exposure (MOE) and Percent of aRfD

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
10.00	0.000000	0.00	>1,000,000	90.00	0.000706	0.24	42,482
20.00	0.000000	0.00	>1,000,000	95.00	0.001077	0.36	27,844
30.00	0.000000	0.00	>1,000,000	97.50	0.002313	0.77	12,967
40.00	0.000000	0.00	>1,000,000	99.00	0.003256	1.09	9,213
50.00	0.000035	0.01	868,877	99.50	0.004411	1.47	6,801
60.00	0.000104	0.03	287,107	99.75	0.004607	1.54	6,511
70.00	0.000202	0.07	148,707	99.90	0.007122	2.37	4,212
80.00	0.000419	0.14	71,615				

Residue file: Dicrotophos acute food+water ppb.R10
Adjustment factor #2 NOT used.
Analysis Date: 12-14-2016/09:36:58 Residue file dated: 12-14-2016/09:05:28
NOEL (Acute) = 30.000000 mg/kg body-wt/day
Acute Reference Dose (aRfD) = 0.300000 mg/kg body-wt/day
RAC/FF intake summed over 24 hours
MC iterations = 100; MC list in residue file; MC seed = 1; RNG = MS VB
Run Comment: "Dose in ug/kg/day, Residue in ppb"
==========

Non-Nursing Infants

	Daily Exposure Analysis (mg/kg body-weight/day) per Capita	per User
Mean	0.000898	0.000918
Standard Deviation	0.001087	0.001091
Margin of Exposure	33,413	32,686
Percent of aRfD	0.30	0.31

Percent of Person-Days that are User-Days = 97.83%

Estimated percentile of user-days falling below calculated exposure in mg/kg body-wt/day with Margin of Exposure (MOE) and Percent of aRfD

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
10.00	0.000108	0.04	277,036	90.00	0.001674	0.56	17,915
20.00	0.000250	0.08	119,950	95.00	0.002399	0.80	12,503
30.00	0.000462	0.15	64,885	97.50	0.003504	1.17	8,561
40.00	0.000586	0.20	51,186	99.00	0.005411	1.80	5,544
50.00	0.000709	0.24	42,322	99.50	0.009711	3.24	3,089
60.00	0.000840	0.28	35,693	99.75	0.010874	3.62	2,758
70.00	0.000996	0.33	30,120	99.90	0.011293	3.76	2,656
80.00	0.001213	0.40	24,733				

Estimated percentile of per-capita days falling below calculated exposure in mg/kg body-wt/day with Margin of Exposure (MOE) and Percent of aRfD

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
10.00	0.000096	0.03	313,606	90.00	0.001655	0.55	18,131
20.00	0.000196	0.07	153,315	95.00	0.002386	0.80	12,571
30.00	0.000435	0.15	68,944	97.50	0.003481	1.16	8,618
40.00	0.000570	0.19	52,591	99.00	0.005398	1.80	5,557
50.00	0.000697	0.23	43,062	99.50	0.009476	3.16	3,165
60.00	0.000829	0.28	36,170	99.75	0.010870	3.62	2,759
70.00	0.000984	0.33	30,496	99.90	0.011290	3.76	2,657
80.00	0.001192	0.40	25,174				

Residue file: Dicrotophos acute food+water ppb.R10
Adjustment factor #2 NOT used.
Analysis Date: 12-14-2016/09:36:58 Residue file dated: 12-14-2016/09:05:28
NOEL (Acute) = 30.000000 mg/kg body-wt/day
Acute Reference Dose (aRfD) = 0.300000 mg/kg body-wt/day
RAC/FF intake summed over 24 hours
MC iterations = 100; MC list in residue file; MC seed = 1; RNG = MS VB
Run Comment: "Dose in ug/kg/day, Residue in ppb"
==========

Female 13+ PREG

	Daily Exposure Analysis (mg/kg body-weight/day) per Capita	per User
Mean	0.000989	0.000989
Standard Deviation	0.001418	0.001418
Margin of Exposure	30,344	30,344
Percent of aRfD	0.33	0.33

Percent of Person-Days that are User-Days = 100.00%

Estimated percentile of user-days falling below calculated exposure in mg/kg body-wt/day with Margin of Exposure (MOE) and Percent of aRfD

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
10.00	0.000181	0.06	165,958	90.00	0.002031	0.68	14,770
20.00	0.000321	0.11	93,570	95.00	0.002432	0.81	12,334
30.00	0.000448	0.15	66,925	97.50	0.003192	1.06	9,399
40.00	0.000588	0.20	51,004	99.00	0.004463	1.49	6,722
50.00	0.000722	0.24	41,536	99.50	0.004599	1.53	6,522
60.00	0.000886	0.30	33,862	99.75	0.004691	1.56	6,395
70.00	0.001152	0.38	26,031	99.90	0.004784	1.59	6,271
80.00	0.001498	0.50	20,021				

Estimated percentile of per-capita days falling below calculated exposure in mg/kg body-wt/day with Margin of Exposure (MOE) and Percent of aRfD

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
10.00	0.000181	0.06	165,958	90.00	0.002031	0.68	14,770
20.00	0.000321	0.11	93,570	95.00	0.002432	0.81	12,334
30.00	0.000448	0.15	66,925	97.50	0.003192	1.06	9,399
40.00	0.000588	0.20	51,004	99.00	0.004463	1.49	6,722
50.00	0.000722	0.24	41,536	99.50	0.004599	1.53	6,522
60.00	0.000886	0.30	33,862	99.75	0.004691	1.56	6,395
70.00	0.001152	0.38	26,031	99.90	0.004784	1.59	6,271
80.00	0.001498	0.50	20,021				

Residue file: Dicrotophos acute food+water ppb.R10
Adjustment factor #2 NOT used.
Analysis Date: 12-14-2016/09:36:58 Residue file dated: 12-14-2016/09:05:28
NOEL (Acute) = 30.000000 mg/kg body-wt/day
Acute Reference Dose (aRfD) = 0.300000 mg/kg body-wt/day
RAC/FF intake summed over 24 hours
MC iterations = 100; MC list in residue file; MC seed = 1; RNG = MS VB
Run Comment: "Dose in ug/kg/day, Residue in ppb"
==========

All Infants

	Daily Exposure Analysis (mg/kg body-weight/day) per Capita	per User
Mean	0.000703	0.000818
Standard Deviation	0.001018	0.001054
Margin of Exposure	42,669	36,693
Percent of aRfD	0.23	0.27

Percent of Person-Days that are User-Days = 85.99%

Estimated percentile of user-days falling below calculated exposure in mg/kg body-wt/day with Margin of Exposure (MOE) and Percent of aRfD

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
10.00	0.000078	0.03	384,094	90.00	0.001593	0.53	18,835
20.00	0.000140	0.05	214,520	95.00	0.002352	0.78	12,756
30.00	0.000315	0.11	95,169	97.50	0.003375	1.13	8,888
40.00	0.000475	0.16	63,103	99.00	0.005032	1.68	5,961
50.00	0.000606	0.20	49,506	99.50	0.006712	2.24	4,469
60.00	0.000741	0.25	40,496	99.75	0.010877	3.63	2,758
70.00	0.000907	0.30	33,078	99.90	0.011326	3.78	2,648
80.00	0.001124	0.37	26,687				

Estimated percentile of per-capita days falling below calculated exposure in mg/kg body-wt/day with Margin of Exposure (MOE) and Percent of aRfD

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
10.00	0.000000	0.00	>1,000,000	90.00	0.001487	0.50	20,168
20.00	0.000058	0.02	514,726	95.00	0.002177	0.73	13,780
30.00	0.000129	0.04	233,342	97.50	0.003161	1.05	9,491
40.00	0.000320	0.11	93,663	99.00	0.004755	1.59	6,308
50.00	0.000500	0.17	59,988	99.50	0.005691	1.90	5,271
60.00	0.000652	0.22	46,025	99.75	0.010831	3.61	2,769
70.00	0.000822	0.27	36,491	99.90	0.011301	3.77	2,654
80.00	0.001041	0.35	28,815				

Residue file: Dicrotophos acute food+water ppb.R10
Adjustment factor #2 NOT used.
Analysis Date: 12-14-2016/09:36:58 Residue file dated: 12-14-2016/09:05:28
NOEL (Acute) = 30.000000 mg/kg body-wt/day
Acute Reference Dose (aRfD) = 0.300000 mg/kg body-wt/day
RAC/FF intake summed over 24 hours
MC iterations = 100; MC list in residue file; MC seed = 1; RNG = MS VB
Run Comment: "Dose in ug/kg/day, Residue in ppb"
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Children 1-2

	Daily Exposure Analysis (mg/kg body-weight/day) per Capita	per User
Mean	0.002615	0.002633
Standard Deviation	0.004375	0.004384
Margin of Exposure	11,473	11,393
Percent of aRfD	0.87	0.88

Percent of Person-Days that are User-Days = 99.31%

Estimated percentile of user-days falling below calculated exposure in mg/kg body-wt/day with Margin of Exposure (MOE) and Percent of aRfD

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
10.00	0.000400	0.13	75,062	90.00	0.005308	1.77	5,652
20.00	0.000692	0.23	43,341	95.00	0.007043	2.35	4,259
30.00	0.001002	0.33	29,951	97.50	0.009127	3.04	3,286
40.00	0.001318	0.44	22,761	99.00	0.013657	4.55	2,196
50.00	0.001710	0.57	17,543	99.50	0.024548	8.18	1,222
60.00	0.002147	0.72	13,970	99.75	0.036144	12.05	830
70.00	0.002803	0.93	10,702	99.90	0.058694	19.56	511
80.00	0.003718	1.24	8,069				

Estimated percentile of per-capita days falling below calculated exposure in mg/kg body-wt/day with Margin of Exposure (MOE) and Percent of aRfD

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
10.00	0.000376	0.13	79,851	90.00	0.005286	1.76	5,675
20.00	0.000677	0.23	44,332	95.00	0.007032	2.34	4,266
30.00	0.000987	0.33	30,400	97.50	0.009115	3.04	3,291
40.00	0.001305	0.44	22,985	99.00	0.013638	4.55	2,199
50.00	0.001698	0.57	17,663	99.50	0.024542	8.18	1,222
60.00	0.002137	0.71	14,038	99.75	0.036120	12.04	830
70.00	0.002789	0.93	10,756	99.90	0.058689	19.56	511
80.00	0.003700	1.23	8,107				

Residue file: Dicrotophos acute food+water ppb.R10
Adjustment factor #2 NOT used.
Analysis Date: 12-14-2016/09:36:58 Residue file dated: 12-14-2016/09:05:28
NOEL (Acute) = 30.000000 mg/kg body-wt/day
Acute Reference Dose (aRfD) = 0.300000 mg/kg body-wt/day
RAC/FF intake summed over 24 hours
MC iterations = 100; MC list in residue file; MC seed = 1; RNG = MS VB
Run Comment: "Dose in ug/kg/day, Residue in ppb"
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Children 3-5

	Daily Exposure Analysis (mg/kg body-weight/day) per Capita	per User
Mean	0.002842	0.002846
Standard Deviation	0.004236	0.004237
Margin of Exposure	10,555	10,541
Percent of aRfD	0.95	0.95

Percent of Person-Days that are User-Days = 99.87%

Estimated percentile of user-days falling below calculated exposure in mg/kg body-wt/day with Margin of Exposure (MOE) and Percent of aRfD

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
10.00	0.000553	0.18	54,222	90.00	0.005167	1.72	5,806
20.00	0.000908	0.30	33,021	95.00	0.006708	2.24	4,471
30.00	0.001315	0.44	22,814	97.50	0.008764	2.92	3,422
40.00	0.001700	0.57	17,648	99.00	0.018954	6.32	1,582
50.00	0.002128	0.71	14,099	99.50	0.021724	7.24	1,380
60.00	0.002605	0.87	11,516	99.75	0.048071	16.02	624
70.00	0.003115	1.04	9,631	99.90	0.063939	21.31	469
80.00	0.003815	1.27	7,864				

Estimated percentile of per-capita days falling below calculated exposure in mg/kg body-wt/day with Margin of Exposure (MOE) and Percent of aRfD

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
10.00	0.000549	0.18	54,648	90.00	0.005165	1.72	5,808
20.00	0.000905	0.30	33,150	95.00	0.006707	2.24	4,473
30.00	0.001312	0.44	22,864	97.50	0.008755	2.92	3,426
40.00	0.001696	0.57	17,683	99.00	0.018952	6.32	1,582
50.00	0.002124	0.71	14,121	99.50	0.021723	7.24	1,381
60.00	0.002603	0.87	11,525	99.75	0.048066	16.02	624
70.00	0.003113	1.04	9,638	99.90	0.063937	21.31	469
80.00	0.003813	1.27	7,867				

Residue file: Dicrotophos acute food+water ppb.R10
Adjustment factor #2 NOT used.
Analysis Date: 12-14-2016/09:36:58 Residue file dated: 12-14-2016/09:05:28
NOEL (Acute) = 30.000000 mg/kg body-wt/day
Acute Reference Dose (aRfD) = 0.300000 mg/kg body-wt/day
RAC/FF intake summed over 24 hours
MC iterations = 100; MC list in residue file; MC seed = 1; RNG = MS VB
Run Comment: "Dose in ug/kg/day, Residue in ppb"
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Children 6-12

	Daily Exposure Analysis (mg/kg body-weight/day) per Capita	per User
Mean	0.002060	0.002061
Standard Deviation	0.002835	0.002835
Margin of Exposure	14,564	14,555
Percent of aRfD	0.69	0.69

Percent of Person-Days that are User-Days = 99.94%

Estimated percentile of user-days falling below calculated exposure in mg/kg body-wt/day with Margin of Exposure (MOE) and Percent of aRfD

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
10.00	0.000371	0.12	80,818	90.00	0.003887	1.30	7,718
20.00	0.000652	0.22	46,032	95.00	0.005284	1.76	5,677
30.00	0.000928	0.31	32,326	97.50	0.006954	2.32	4,314
40.00	0.001187	0.40	25,276	99.00	0.012105	4.03	2,478
50.00	0.001469	0.49	20,423	99.50	0.017659	5.89	1,698
60.00	0.001824	0.61	16,450	99.75	0.029146	9.72	1,029
70.00	0.002225	0.74	13,481	99.90	0.042377	14.13	707
80.00	0.002795	0.93	10,733				

Estimated percentile of per-capita days falling below calculated exposure in mg/kg body-wt/day with Margin of Exposure (MOE) and Percent of aRfD

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
10.00	0.000369	0.12	81,212	90.00	0.003885	1.30	7,721
20.00	0.000651	0.22	46,108	95.00	0.005282	1.76	5,679
30.00	0.000927	0.31	32,363	97.50	0.006953	2.32	4,314
40.00	0.001186	0.40	25,301	99.00	0.012102	4.03	2,478
50.00	0.001468	0.49	20,437	99.50	0.017657	5.89	1,699
60.00	0.001823	0.61	16,459	99.75	0.029145	9.71	1,029
70.00	0.002225	0.74	13,485	99.90	0.042376	14.13	707
80.00	0.002794	0.93	10,736				

Residue file: Dicrotophos acute food+water ppb.R10
Adjustment factor #2 NOT used.
Analysis Date: 12-14-2016/09:36:58 Residue file dated: 12-14-2016/09:05:28
NOEL (Acute) = 30.000000 mg/kg body-wt/day
Acute Reference Dose (aRfD) = 0.300000 mg/kg body-wt/day
RAC/FF intake summed over 24 hours
MC iterations = 100; MC list in residue file; MC seed = 1; RNG = MS VB
Run Comment: "Dose in ug/kg/day, Residue in ppb"

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Youth 13-19

	Daily Exposure Analysis (mg/kg body-weight/day) per Capita	per User
Mean	0.001284	0.001286
Standard Deviation	0.001799	0.001800
Margin of Exposure	23,369	23,326
Percent of aRfD	0.43	0.43

Percent of Person-Days that are User-Days = 99.82%

Estimated percentile of user-days falling below calculated exposure in mg/kg body-wt/day with Margin of Exposure (MOE) and Percent of aRfD

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
10.00	0.000203	0.07	147,587	90.00	0.002462	0.82	12,183
20.00	0.000371	0.12	80,899	95.00	0.003387	1.13	8,858
30.00	0.000529	0.18	56,756	97.50	0.004735	1.58	6,335
40.00	0.000708	0.24	42,386	99.00	0.007164	2.39	4,187
50.00	0.000895	0.30	33,514	99.50	0.011947	3.98	2,511
60.00	0.001115	0.37	26,899	99.75	0.019082	6.36	1,572
70.00	0.001389	0.46	21,602	99.90	0.021337	7.11	1,406
80.00	0.001791	0.60	16,746				

Estimated percentile of per-capita days falling below calculated exposure in mg/kg body-wt/day with Margin of Exposure (MOE) and Percent of aRfD

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
10.00	0.000201	0.07	149,344	90.00	0.002460	0.82	12,194
20.00	0.000368	0.12	81,430	95.00	0.003384	1.13	8,866
30.00	0.000527	0.18	56,966	97.50	0.004732	1.58	6,340
40.00	0.000706	0.24	42,512	99.00	0.007157	2.39	4,191
50.00	0.000893	0.30	33,599	99.50	0.011944	3.98	2,511
60.00	0.001113	0.37	26,947	99.75	0.019082	6.36	1,572
70.00	0.001387	0.46	21,628	99.90	0.021335	7.11	1,406
80.00	0.001790	0.60	16,763				

Residue file: Dicrotophos acute food+water ppb.R10
Adjustment factor #2 NOT used.
Analysis Date: 12-14-2016/09:36:58 Residue file dated: 12-14-2016/09:05:28
NOEL (Acute) = 30.000000 mg/kg body-wt/day
Acute Reference Dose (aRfD) = 0.300000 mg/kg body-wt/day
RAC/FF intake summed over 24 hours
MC iterations = 100; MC list in residue file; MC seed = 1; RNG = MS VB
Run Comment: "Dose in ug/kg/day, Residue in ppb"
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Adults 20-49

	Daily Exposure Analysis (mg/kg body-weight/day) per Capita	per User
Mean	0.000933	0.000934
Standard Deviation	0.001362	0.001363
Margin of Exposure	32,157	32,126
Percent of aRfD	0.31	0.31

Percent of Person-Days that are User-Days = 99.90%

Estimated percentile of user-days falling below calculated exposure in mg/kg body-wt/day with Margin of Exposure (MOE) and Percent of aRfD

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
10.00	0.000172	0.06	174,235	90.00	0.001804	0.60	16,633
20.00	0.000290	0.10	103,475	95.00	0.002370	0.79	12,660
30.00	0.000408	0.14	73,526	97.50	0.003104	1.03	9,664
40.00	0.000534	0.18	56,198	99.00	0.004478	1.49	6,699
50.00	0.000672	0.22	44,621	99.50	0.006269	2.09	4,785
60.00	0.000832	0.28	36,074	99.75	0.010176	3.39	2,948
70.00	0.001037	0.35	28,922	99.90	0.020639	6.88	1,453
80.00	0.001319	0.44	22,748				

Estimated percentile of per-capita days falling below calculated exposure in mg/kg body-wt/day with Margin of Exposure (MOE) and Percent of aRfD

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
10.00	0.000171	0.06	175,279	90.00	0.001803	0.60	16,641
20.00	0.000289	0.10	103,786	95.00	0.002369	0.79	12,664
30.00	0.000407	0.14	73,663	97.50	0.003103	1.03	9,667
40.00	0.000533	0.18	56,293	99.00	0.004477	1.49	6,701
50.00	0.000672	0.22	44,671	99.50	0.006260	2.09	4,792
60.00	0.000831	0.28	36,103	99.75	0.010174	3.39	2,948
70.00	0.001037	0.35	28,943	99.90	0.020638	6.88	1,453
80.00	0.001318	0.44	22,758				

Residue file: Dicrotophos acute food+water ppb.R10
Adjustment factor #2 NOT used.
Analysis Date: 12-14-2016/09:36:58 Residue file dated: 12-14-2016/09:05:28
NOEL (Acute) = 30.000000 mg/kg body-wt/day
Acute Reference Dose (aRfD) = 0.300000 mg/kg body-wt/day
RAC/FF intake summed over 24 hours
MC iterations = 100; MC list in residue file; MC seed = 1; RNG = MS VB
Run Comment: "Dose in ug/kg/day, Residue in ppb"
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Adults 50-99

	Daily Exposure Analysis (mg/kg body-weight/day) per Capita	per User
Mean	0.000727	0.000727
Standard Deviation	0.000747	0.000747
Margin of Exposure	41,286	41,256
Percent of aRfD	0.24	0.24

Percent of Person-Days that are User-Days = 99.93%

Estimated percentile of user-days falling below calculated exposure in mg/kg body-wt/day with Margin of Exposure (MOE) and Percent of aRfD

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
10.00	0.000148	0.05	202,067	90.00	0.001473	0.49	20,366
20.00	0.000240	0.08	124,774	95.00	0.001892	0.63	15,855
30.00	0.000326	0.11	92,040	97.50	0.002465	0.82	12,171
40.00	0.000425	0.14	70,614	99.00	0.003337	1.11	8,988
50.00	0.000541	0.18	55,403	99.50	0.004383	1.46	6,845
60.00	0.000673	0.22	44,559	99.75	0.005874	1.96	5,107
70.00	0.000834	0.28	35,960	99.90	0.008242	2.75	3,639
80.00	0.001065	0.35	28,173				

Estimated percentile of per-capita days falling below calculated exposure in mg/kg body-wt/day with Margin of Exposure (MOE) and Percent of aRfD

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
10.00	0.000148	0.05	202,955	90.00	0.001473	0.49	20,371
20.00	0.000240	0.08	125,001	95.00	0.001892	0.63	15,860
30.00	0.000325	0.11	92,168	97.50	0.002464	0.82	12,174
40.00	0.000424	0.14	70,686	99.00	0.003336	1.11	8,992
50.00	0.000541	0.18	55,451	99.50	0.004382	1.46	6,846
60.00	0.000673	0.22	44,585	99.75	0.005873	1.96	5,107
70.00	0.000834	0.28	35,981	99.90	0.008241	2.75	3,640
80.00	0.001064	0.35	28,184				

Residue file: Dicrotophos acute food+water ppb.R10
Adjustment factor #2 NOT used.
Analysis Date: 12-14-2016/09:36:58 Residue file dated: 12-14-2016/09:05:28
NOEL (Acute) = 30.000000 mg/kg body-wt/day
Acute Reference Dose (aRfD) = 0.300000 mg/kg body-wt/day
RAC/FF intake summed over 24 hours
MC iterations = 100; MC list in residue file; MC seed = 1; RNG = MS VB
Run Comment: "Dose in ug/kg/day, Residue in ppb"
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Female 13-49

	Daily Exposure Analysis (mg/kg body-weight/day) per Capita	per User
Mean	0.000906	0.000907
Standard Deviation	0.001219	0.001220
Margin of Exposure	33,106	33,081
Percent of aRfD	0.30	0.30

Percent of Person-Days that are User-Days = 99.92%

Estimated percentile of user-days falling below calculated exposure in mg/kg body-wt/day with Margin of Exposure (MOE) and Percent of aRfD

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
10.00	0.000162	0.05	185,487	90.00	0.001793	0.60	16,729
20.00	0.000278	0.09	107,833	95.00	0.002343	0.78	12,804
30.00	0.000392	0.13	76,480	97.50	0.003223	1.07	9,308
40.00	0.000513	0.17	58,484	99.00	0.004650	1.55	6,451
50.00	0.000645	0.22	46,499	99.50	0.005995	2.00	5,003
60.00	0.000805	0.27	37,258	99.75	0.008636	2.88	3,473
70.00	0.001008	0.34	29,750	99.90	0.014243	4.75	2,106
80.00	0.001290	0.43	23,255				

Estimated percentile of per-capita days falling below calculated exposure in mg/kg body-wt/day with Margin of Exposure (MOE) and Percent of aRfD

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
10.00	0.000161	0.05	186,491	90.00	0.001793	0.60	16,734
20.00	0.000278	0.09	108,081	95.00	0.002342	0.78	12,809
30.00	0.000392	0.13	76,612	97.50	0.003222	1.07	9,310
40.00	0.000512	0.17	58,539	99.00	0.004647	1.55	6,455
50.00	0.000645	0.21	46,541	99.50	0.005995	2.00	5,004
60.00	0.000805	0.27	37,284	99.75	0.008635	2.88	3,474
70.00	0.001008	0.34	29,767	99.90	0.014240	4.75	2,106
80.00	0.001290	0.43	23,263				

Residue file: Dicrotophos acute food+water ppb.R10
Adjustment factor #2 NOT used.
Analysis Date: 12-14-2016/09:36:58 Residue file dated: 12-14-2016/09:05:28
NOEL (Acute) = 30.000000 mg/kg body-wt/day
Acute Reference Dose (aRfD) = 0.300000 mg/kg body-wt/day
RAC/FF intake summed over 24 hours
MC iterations = 100; MC list in residue file; MC seed = 1; RNG = MS VB
Run Comment: "Dose in ug/kg/day, Residue in ppb"
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Custom demographics 1: Adults, 18+ yrs
Sex: M/F-all/
All Races
Age-Low: 18 yrs High: 99 yrs

	Daily Exposure Analysis (mg/kg body-weight/day) per Capita	per User
Mean	0.000858	0.000859
Standard Deviation	0.001167	0.001167
Margin of Exposure	34,963	34,933
Percent of aRfD	0.29	0.29

Percent of Person-Days that are User-Days = 99.91%

Estimated percentile of user-days falling below calculated exposure in mg/kg body-wt/day with Margin of Exposure (MOE) and Percent of aRfD

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
10.00	0.000162	0.05	185,508	90.00	0.001703	0.57	17,612
20.00	0.000267	0.09	112,422	95.00	0.002216	0.74	13,537
30.00	0.000372	0.12	80,594	97.50	0.002912	0.97	10,302
40.00	0.000488	0.16	61,523	99.00	0.004265	1.42	7,033
50.00	0.000618	0.21	48,537	99.50	0.005731	1.91	5,234
60.00	0.000769	0.26	39,029	99.75	0.008313	2.77	3,608
70.00	0.000957	0.32	31,357	99.90	0.016997	5.67	1,765
80.00	0.001228	0.41	24,423				

Estimated percentile of per-capita days falling below calculated exposure in mg/kg body-wt/day with Margin of Exposure (MOE) and Percent of aRfD

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
10.00	0.000161	0.05	186,557	90.00	0.001703	0.57	17,619
20.00	0.000266	0.09	112,702	95.00	0.002215	0.74	13,541
30.00	0.000372	0.12	80,731	97.50	0.002911	0.97	10,304
40.00	0.000487	0.16	61,607	99.00	0.004264	1.42	7,035
50.00	0.000618	0.21	48,581	99.50	0.005729	1.91	5,236
60.00	0.000768	0.26	39,058	99.75	0.008311	2.77	3,609
70.00	0.000956	0.32	31,375	99.90	0.016995	5.67	1,765
80.00	0.001228	0.41	24,435				

Ver. 4.02, 05-10-c

DEEM-FCID Acute analysis for DICROTOPHOS
Residue file name: H:\MyFiles\DEEM-FCID Files\Dicrotophos\Dicrotophos v4.02 Files\Dicrotophos acute food+water ppb.R10
Analysis Date 12-14-2016 Residue file dated: 12-14-2016/09:05:28
Reference dose: aRfD = 0.25 mg/kg bw/day NOEL = 25 mg/kg bw/day
Comment: Dose in ug/kg/day, Residue in ppb

RDL indices and parameters for Monte Carlo Analysis:

Index #	Dist Code	Parameter #1	Param #2	Param #3	Comment
1	6	Drinking Water ppb.rdf			

EPA Code	Crop Grp	Food Name	Def Res (ppm)	Adj.Factors #1	#2	RDL Pntr	Comment
2003128000	20C	Cottonseed, oil	40.000000	1.000	1.000		residu
Full comment: residue in ppb							
2003128001	20C	Cottonseed, oil-babyfood	40.000000	1.000	1.000		residu
Full comment: residue in ppb							
8601000000	86A	Water, direct, all sources	0.009000	1.000	1.000	1	residu
Full comment: residue in ppb							
8602000000	86B	Water, indirect, all sources	0.009000	1.000	1.000	1	residu
Full comment: residue in ppb							

Summary of Residue Distribution Files (RDF) listed in H:\MyFiles\DEEM-FCID Files\Dicrotophos\Dicrotophos v4.02 Files\Dicrotophos acute food+water ppb.R10

RDF #	File Name	N residues w freq's	N residues w/o freq's	N LODs	LOD Value	N Zeros
1	Drinking Water ppb.rdf	0	400	0	0	0

Ver. 4.02, 05-10-c
DEEM-FCID ACUTE Analysis for DICROTOPHOS NHANES 2005-2010 2-Day
Residue file: Dicrotophos acute food+water ppb.R10
Adjustment factor #2 NOT used.
Analysis Date: 12-14-2016/15:54:04 Residue file dated: 12-14-2016/09:05:28
NOEL (Acute) = 25.000000 mg/kg body-wt/day
Two-Day Average Results Reported
RAC/FF intake summed over 24 hours
MC iterations = 100; MC list in residue file; MC seed = 1; RNG = MS VB
Run Comment: "Dose in ug/kg/day, Residue in ppb"
==========

Summary calculations--per capita:

--- 95th Percentile----			--- 97.5th Percentile----			---99.9th Percentile----		
Exposure	% aRfD	MOE	Exposure	% aRfD	MOE	Exposure	% aRfD	MOE
Total US Population:								
0.003077	1.23	8124	0.004085	1.63	6120	0.018723	7.49	1335
Nursing Infants:								
0.001238	0.50	20199	0.001805	0.72	13849	0.004870	1.95	5133
Non-Nursing Infants:								
0.002363	0.95	10580	0.003288	1.32	7604	0.007850	3.14	3184
Female 13+ PREG:								
0.002326	0.93	10748	0.003174	1.27	7876	0.025848	10.34	967
All Infants:								
0.001958	0.78	12769	0.003141	1.26	7959	0.007686	3.07	3252
Children 1-2:								
0.006346	2.54	3939	0.008374	3.35	2985	0.041619	16.65	600
Children 3-5:								
0.006171	2.47	4051	0.009626	3.85	2597	0.042827	17.13	583
Children 6-12:								
0.004765	1.91	5246	0.006373	2.55	3923	0.026499	10.60	943
Youth 13-19:								
0.003101	1.24	8060	0.003965	1.59	6304	0.016051	6.42	1557
Adults 20-49:								
0.002156	0.86	11594	0.002704	1.08	9244	0.013102	5.24	1908
Adults 50-99:								
0.001737	0.69	14392	0.002087	0.83	11979	0.006868	2.75	3640
Female 13-49:								
0.002174	0.87	11497	0.002844	1.14	8790	0.012175	4.87	2053
Custom demographics 1: Adults, 18+ yrs:								
0.002016	0.81	12398	0.002550	1.02	9802	0.010661	4.26	2344

Ver. 4.02, 05-10-c
DEEM-FCID ACUTE Analysis for DICROTOPHOS NHANES 2005-2010 2-Day
Residue file: Dicrotophos acute food+water ppb.R10
Adjustment factor #2 NOT used.
Analysis Date: 12-14-2016/15:54:04 Residue file dated: 12-14-2016/09:05:28
NOEL (Acute) = 25.000000 mg/kg body-wt/day
Two-Day Average Results Reported
RAC/FF intake summed over 24 hours
MC iterations = 100; MC list in residue file; MC seed = 1; RNG = MS VB
Run Comment: "Dose in ug/kg/day, Residue in ppb"
==========

Summary calculations--users:

--- 95th Percentile----			--- 97.5th Percentile----			---99.9th Percentile----		
Exposure	% aRfD	MOE	Exposure	% aRfD	MOE	Exposure	% aRfD	MOE
Total US Population:								
0.003079	1.23	8119	0.004088	1.64	6115	0.018727	7.49	1334
Nursing Infants:								
0.001752	0.70	14267	0.002552	1.02	9796	0.006644	2.66	3762
Non-Nursing Infants:								
0.002408	0.96	10381	0.003292	1.32	7593	0.007853	3.14	3183
Female 13+ PREG:								
0.002326	0.93	10748	0.003174	1.27	7876	0.025848	10.34	967
All Infants:								
0.002183	0.87	11449	0.003260	1.30	7669	0.007697	3.08	3247
Children 1-2:								
0.006350	2.54	3937	0.008385	3.35	2981	0.041621	16.65	600
Children 3-5:								
0.006173	2.47	4049	0.009636	3.85	2594	0.042828	17.13	583
Children 6-12:								
0.004765	1.91	5246	0.006373	2.55	3923	0.026499	10.60	943
Youth 13-19:								
0.003101	1.24	8060	0.003965	1.59	6304	0.016051	6.42	1557
Adults 20-49:								
0.002156	0.86	11594	0.002704	1.08	9244	0.013102	5.24	1908
Adults 50-99:								
0.001737	0.69	14392	0.002087	0.83	11979	0.006868	2.75	3640
Female 13-49:								
0.002174	0.87	11497	0.002844	1.14	8790	0.012175	4.87	2053
Custom demographics 1: Adults, 18+ yrs:								
0.002016	0.81	12398	0.002550	1.02	9802	0.010661	4.26	2344

Ver. 4.02, 05-10-c
DEEM-FCID ACUTE Analysis for DICROTOPHOS NHANES 2005-2010 2-Day
Residue file: Dicrotophos acute food+water ppb.R10
Adjustment factor #2 NOT used.
Analysis Date: 12-14-2016/15:54:04 Residue file dated: 12-14-2016/09:05:28
NOEL (Acute) = 25.000000 mg/kg body-wt/day
Acute Reference Dose (aRfD) = 0.250000 mg/kg body-wt/day
Two-Day Average Results Reported
RAC/FF intake summed over 24 hours
MC iterations = 100; MC list in residue file; MC seed = 1; RNG = MS VB
Run Comment: "Dose in ug/kg/day, Residue in ppb"

Total US Population	2-Day Avg Exposure Analysis /a (mg/kg body-weight/day) per Capita	per User
Mean	0.001130	0.001132
Standard Deviation	0.001485	0.001486
Margin of Exposure 2/	22,123	22,078
Percent of aRfD	0.45	0.45

Percent of Individuals that are Users (over two days) = 99.80%

Estimated percentile of user-days falling below calculated exposure in mg/kg body-wt/day with Margin of Exposure (MOE) and Percent of aRfD

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
10.00	0.000266	0.11	94,037	90.00	0.002204	0.88	11,342
20.00	0.000401	0.16	62,340	95.00	0.003079	1.23	8,119
30.00	0.000522	0.21	47,936	97.50	0.004088	1.64	6,115
40.00	0.000645	0.26	38,780	99.00	0.006030	2.41	4,146
50.00	0.000786	0.31	31,815	99.50	0.008839	3.54	2,828
60.00	0.000955	0.38	26,164	99.75	0.011274	4.51	2,217
70.00	0.001179	0.47	21,212	99.90	0.018727	7.49	1,334
80.00	0.001521	0.61	16,441				

Estimated percentile of per-capita days falling below calculated exposure in mg/kg body-wt/day with Margin of Exposure (MOE) and Percent of aRfD

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
10.00	0.000263	0.11	94,932	90.00	0.002202	0.88	11,353
20.00	0.000399	0.16	62,644	95.00	0.003077	1.23	8,124
30.00	0.000520	0.21	48,106	97.50	0.004085	1.63	6,120
40.00	0.000643	0.26	38,871	99.00	0.006022	2.41	4,151
50.00	0.000784	0.31	31,883	99.50	0.008831	3.53	2,831
60.00	0.000954	0.38	26,207	99.75	0.011255	4.50	2,221
70.00	0.001177	0.47	21,240	99.90	0.018723	7.49	1,335
80.00	0.001519	0.61	16,459				

a/ Analysis based on all two-day participant records in NHANES 2005-2010 2-Day with 2 days of valid drinking water records.
2/ Margin of Exposure = NOEL/ Dietary Exposure.

Residue file: Dicrotophos acute food+water ppb.R10
Adjustment factor #2 NOT used.
Analysis Date: 12-14-2016/15:54:04 Residue file dated: 12-14-2016/09:05:28
NOEL (Acute) = 25.000000 mg/kg body-wt/day
Acute Reference Dose (aRfD) = 0.250000 mg/kg body-wt/day
Two-Day Average Results Reported
RAC/FF intake summed over 24 hours
MC iterations = 100; MC list in residue file; MC seed = 1; RNG = MS VB
Run Comment: "Dose in ug/kg/day, Residue in ppb"
==========

Nursing Infants

2-Day Avg Exposure Analysis (mg/kg body-weight/day)

	per Capita	per User
Mean	0.000279	0.000425
Standard Deviation	0.000599	0.000696
Margin of Exposure	89,664	58,853
Percent of aRfD	0.11	0.17

Percent of Individuals that are Users (over two days) = 65.64%

Estimated percentile of user-days falling below calculated exposure in mg/kg body-wt/day with Margin of Exposure (MOE) and Percent of aRfD

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
10.00	0.000012	0.00	>1,000,000	90.00	0.000922	0.37	27,123
20.00	0.000038	0.02	656,810	95.00	0.001752	0.70	14,267
30.00	0.000081	0.03	309,863	97.50	0.002552	1.02	9,796
40.00	0.000137	0.05	183,055	99.00	0.004029	1.61	6,205
50.00	0.000211	0.08	118,380	99.50	0.004326	1.73	5,778
60.00	0.000303	0.12	82,400	99.75	0.004711	1.88	5,306
70.00	0.000406	0.16	61,600	99.90	0.006644	2.66	3,762
80.00	0.000549	0.22	45,498				

Estimated percentile of per-capita days falling below calculated exposure in mg/kg body-wt/day with Margin of Exposure (MOE) and Percent of aRfD

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
10.00	0.000000	0.00	>1,000,000	90.00	0.000683	0.27	36,628
20.00	0.000000	0.00	>1,000,000	95.00	0.001238	0.50	20,199
30.00	0.000000	0.00	>1,000,000	97.50	0.001805	0.72	13,849
40.00	0.000010	0.00	>1,000,000	99.00	0.003597	1.44	6,950
50.00	0.000053	0.02	476,112	99.50	0.004143	1.66	6,034
60.00	0.000130	0.05	192,367	99.75	0.004682	1.87	5,339
70.00	0.000256	0.10	97,578	99.90	0.004870	1.95	5,133
80.00	0.000402	0.16	62,235				

Residue file: Dicrotophos acute food+water ppb.R10
Adjustment factor #2 NOT used.
Analysis Date: 12-14-2016/15:54:04 Residue file dated: 12-14-2016/09:05:28
NOEL (Acute) = 25.000000 mg/kg body-wt/day
Acute Reference Dose (aRfD) = 0.250000 mg/kg body-wt/day
Two-Day Average Results Reported
RAC/FF intake summed over 24 hours
MC iterations = 100; MC list in residue file; MC seed = 1; RNG = MS VB
Run Comment: "Dose in ug/kg/day, Residue in ppb"
==========

Non-Nursing Infants

2-Day Avg Exposure Analysis (mg/kg body-weight/day)

	per Capita	per User
Mean	0.000897	0.000910
Standard Deviation	0.000962	0.000963
Margin of Exposure	27,883	27,461
Percent of aRfD	0.36	0.36

Percent of Individuals that are Users (over two days) = 98.49%

Estimated percentile of user-days falling below calculated exposure in mg/kg body-wt/day with Margin of Exposure (MOE) and Percent of aRfD

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
10.00	0.000118	0.05	211,763	90.00	0.001609	0.64	15,535
20.00	0.000305	0.12	81,852	95.00	0.002408	0.96	10,381
30.00	0.000503	0.20	49,656	97.50	0.003292	1.32	7,593
40.00	0.000615	0.25	40,635	99.00	0.006627	2.65	3,772
50.00	0.000718	0.29	34,814	99.50	0.007610	3.04	3,285
60.00	0.000847	0.34	29,527	99.75	0.007650	3.06	3,268
70.00	0.001002	0.40	24,951	99.90	0.007853	3.14	3,183
80.00	0.001218	0.49	20,524				

Estimated percentile of per-capita days falling below calculated exposure in mg/kg body-wt/day with Margin of Exposure (MOE) and Percent of aRfD

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
10.00	0.000107	0.04	233,453	90.00	0.001597	0.64	15,653
20.00	0.000251	0.10	99,405	95.00	0.002363	0.95	10,580
30.00	0.000487	0.19	51,315	97.50	0.003288	1.32	7,604
40.00	0.000605	0.24	41,352	99.00	0.006614	2.65	3,779
50.00	0.000710	0.28	35,188	99.50	0.007609	3.04	3,285
60.00	0.000841	0.34	29,733	99.75	0.007649	3.06	3,268
70.00	0.000993	0.40	25,171	99.90	0.007850	3.14	3,184
80.00	0.001211	0.48	20,645				

Ver. 4.02, 05-10-c
DEEM-FCID ACUTE Analysis for DICROTOPHOS NHANES 2005-2010 2-Day
Residue file: Dicrotophos acute food+water ppb.R10
Adjustment factor #2 NOT used.
Analysis Date: 12-14-2016/15:54:04 Residue file dated: 12-14-2016/09:05:28
NOEL (Acute) = 25.000000 mg/kg body-wt/day
Acute Reference Dose (aRfD) = 0.250000 mg/kg body-wt/day
Two-Day Average Results Reported
RAC/FF intake summed over 24 hours
MC iterations = 100; MC list in residue file; MC seed = 1; RNG = MS VB
Run Comment: "Dose in ug/kg/day, Residue in ppb"
==========

Female 13+ PREG

2-Day Avg Exposure Analysis
(mg/kg body-weight/day)

	per Capita	per User
Mean	0.000988	0.000988
Standard Deviation	0.001062	0.001062
Margin of Exposure	25,304	25,304
Percent of aRfD	0.40	0.40

Percent of Individuals that are Users (over two days) = 100.00%

Estimated percentile of user-days falling below calculated exposure
in mg/kg body-wt/day with Margin of Exposure (MOE) and Percent of aRfD

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
10.00	0.000274	0.11	91,297	90.00	0.001779	0.71	14,048
20.00	0.000411	0.16	60,824	95.00	0.002326	0.93	10,748
30.00	0.000565	0.23	44,231	97.50	0.003174	1.27	7,876
40.00	0.000704	0.28	35,517	99.00	0.003286	1.31	7,607
50.00	0.000815	0.33	30,685	99.50	0.003893	1.56	6,421
60.00	0.000931	0.37	26,863	99.75	0.003935	1.57	6,353
70.00	0.001098	0.44	22,767	99.90	0.025848	10.34	967
80.00	0.001395	0.56	17,925				

Estimated percentile of per-capita days falling below calculated exposure
in mg/kg body-wt/day with Margin of Exposure (MOE) and Percent of aRfD

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
10.00	0.000274	0.11	91,297	90.00	0.001779	0.71	14,048
20.00	0.000411	0.16	60,824	95.00	0.002326	0.93	10,748
30.00	0.000565	0.23	44,231	97.50	0.003174	1.27	7,876
40.00	0.000704	0.28	35,517	99.00	0.003286	1.31	7,607
50.00	0.000815	0.33	30,685	99.50	0.003893	1.56	6,421
60.00	0.000931	0.37	26,863	99.75	0.003935	1.57	6,353
70.00	0.001098	0.44	22,767	99.90	0.025848	10.34	967
80.00	0.001395	0.56	17,925				

Residue file: Dicrotophos acute food+water ppb.R10
Adjustment factor #2 NOT used.
Analysis Date: 12-14-2016/15:54:04 Residue file dated: 12-14-2016/09:05:28
NOEL (Acute) = 25.000000 mg/kg body-wt/day
Acute Reference Dose (aRfD) = 0.250000 mg/kg body-wt/day
Two-Day Average Results Reported
RAC/FF intake summed over 24 hours
MC iterations = 100; MC list in residue file; MC seed = 1; RNG = MS VB
Run Comment: "Dose in ug/kg/day, Residue in ppb"
==========

All Infants

2-Day Avg Exposure Analysis
(mg/kg body-weight/day)

	per Capita	per User
Mean	0.000702	0.000797
Standard Deviation	0.000911	0.000930
Margin of Exposure	35,598	31,382
Percent of aRfD	0.28	0.32

Percent of Individuals that are Users (over two days) = 88.16%

Estimated percentile of user-days falling below calculated exposure in mg/kg body-wt/day with Margin of Exposure (MOE) and Percent of aRfD

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
10.00	0.000079	0.03	314,537	90.00	0.001539	0.62	16,239
20.00	0.000145	0.06	172,336	95.00	0.002183	0.87	11,449
30.00	0.000321	0.13	77,954	97.50	0.003260	1.30	7,669
40.00	0.000489	0.20	51,084	99.00	0.004339	1.74	5,761
50.00	0.000614	0.25	40,722	99.50	0.007556	3.02	3,308
60.00	0.000745	0.30	33,571	99.75	0.007610	3.04	3,285
70.00	0.000889	0.36	28,116	99.90	0.007697	3.08	3,247
80.00	0.001132	0.45	22,084				

Estimated percentile of per-capita days falling below calculated exposure in mg/kg body-wt/day with Margin of Exposure (MOE) and Percent of aRfD

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
10.00	0.000000	0.00	>1,000,000	90.00	0.001475	0.59	16,949
20.00	0.000074	0.03	340,065	95.00	0.001958	0.78	12,769
30.00	0.000150	0.06	166,584	97.50	0.003141	1.26	7,959
40.00	0.000356	0.14	70,184	99.00	0.004072	1.63	6,139
50.00	0.000535	0.21	46,734	99.50	0.007454	2.98	3,353
60.00	0.000674	0.27	37,085	99.75	0.007603	3.04	3,288
70.00	0.000838	0.34	29,834	99.90	0.007686	3.07	3,252
80.00	0.001053	0.42	23,741				

Residue file: Dicrotophos acute food+water ppb.R10
Adjustment factor #2 NOT used.
Analysis Date: 12-14-2016/15:54:04 Residue file dated: 12-14-2016/09:05:28
NOEL (Acute) = 25.000000 mg/kg body-wt/day
Acute Reference Dose (aRfD) = 0.250000 mg/kg body-wt/day
Two-Day Average Results Reported
RAC/FF intake summed over 24 hours
MC iterations = 100; MC list in residue file; MC seed = 1; RNG = MS VB
Run Comment: "Dose in ug/kg/day, Residue in ppb"
==========

Children 1-2

2-Day Avg Exposure Analysis
(mg/kg body-weight/day)

	per Capita	per User
Mean	0.002614	0.002625
Standard Deviation	0.003369	0.003372
Margin of Exposure	9,563	9,522
Percent of aRfD	1.05	1.05

Percent of Individuals that are Users (over two days) = 99.57%

Estimated percentile of user-days falling below calculated exposure in mg/kg body-wt/day with Margin of Exposure (MOE) and Percent of aRfD

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
10.00	0.000649	0.26	38,509	90.00	0.005007	2.00	4,992
20.00	0.000923	0.37	27,070	95.00	0.006350	2.54	3,937
30.00	0.001215	0.49	20,575	97.50	0.008385	3.35	2,981
40.00	0.001546	0.62	16,170	99.00	0.013222	5.29	1,890
50.00	0.001909	0.76	13,097	99.50	0.018687	7.47	1,337
60.00	0.002305	0.92	10,846	99.75	0.033465	13.39	747
70.00	0.002868	1.15	8,716	99.90	0.041621	16.65	600
80.00	0.003648	1.46	6,853				

Estimated percentile of per-capita days falling below calculated exposure in mg/kg body-wt/day with Margin of Exposure (MOE) and Percent of aRfD

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
10.00	0.000639	0.26	39,152	90.00	0.005001	2.00	4,999
20.00	0.000914	0.37	27,342	95.00	0.006346	2.54	3,939
30.00	0.001208	0.48	20,703	97.50	0.008374	3.35	2,985
40.00	0.001530	0.61	16,337	99.00	0.013220	5.29	1,891
50.00	0.001904	0.76	13,133	99.50	0.018679	7.47	1,338
60.00	0.002298	0.92	10,878	99.75	0.033462	13.38	747
70.00	0.002862	1.14	8,736	99.90	0.041619	16.65	600
80.00	0.003627	1.45	6,893				

Residue file: Dicrotophos acute food+water ppb.R10
Adjustment factor #2 NOT used.
Analysis Date: 12-14-2016/15:54:04 Residue file dated: 12-14-2016/09:05:28
NOEL (Acute) = 25.000000 mg/kg body-wt/day
Acute Reference Dose (aRfD) = 0.250000 mg/kg body-wt/day
Two-Day Average Results Reported
RAC/FF intake summed over 24 hours
MC iterations = 100; MC list in residue file; MC seed = 1; RNG = MS VB
Run Comment: "Dose in ug/kg/day, Residue in ppb"
==========

Children 3-5

2-Day Avg Exposure Analysis
(mg/kg body-weight/day)

	per Capita	per User
Mean	0.002843	0.002846
Standard Deviation	0.003131	0.003131
Margin of Exposure	8,793	8,783
Percent of aRfD	1.14	1.14

Percent of Individuals that are Users (over two days) = 99.89%

Estimated percentile of user-days falling below calculated exposure in mg/kg body-wt/day with Margin of Exposure (MOE) and Percent of aRfD

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
10.00	0.000892	0.36	28,040	90.00	0.004630	1.85	5,399
20.00	0.001272	0.51	19,656	95.00	0.006173	2.47	4,049
30.00	0.001617	0.65	15,457	97.50	0.009636	3.85	2,594
40.00	0.001944	0.78	12,862	99.00	0.011724	4.69	2,132
50.00	0.002279	0.91	10,969	99.50	0.024921	9.97	1,003
60.00	0.002664	1.07	9,385	99.75	0.034581	13.83	722
70.00	0.003083	1.23	8,109	99.90	0.042828	17.13	583
80.00	0.003739	1.50	6,686				

Estimated percentile of per-capita days falling below calculated exposure in mg/kg body-wt/day with Margin of Exposure (MOE) and Percent of aRfD

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
10.00	0.000888	0.36	28,140	90.00	0.004628	1.85	5,402
20.00	0.001269	0.51	19,707	95.00	0.006171	2.47	4,051
30.00	0.001615	0.65	15,480	97.50	0.009626	3.85	2,597
40.00	0.001942	0.78	12,871	99.00	0.011724	4.69	2,132
50.00	0.002276	0.91	10,982	99.50	0.024919	9.97	1,003
60.00	0.002662	1.06	9,390	99.75	0.034579	13.83	722
70.00	0.003081	1.23	8,114	99.90	0.042827	17.13	583
80.00	0.003737	1.49	6,689				

Residue file: Dicrotophos acute food+water ppb.R10
Adjustment factor #2 NOT used.
Analysis Date: 12-14-2016/15:54:04 Residue file dated: 12-14-2016/09:05:28
NOEL (Acute) = 25.000000 mg/kg body-wt/day
Acute Reference Dose (aRfD) = 0.250000 mg/kg body-wt/day
Two-Day Average Results Reported
RAC/FF intake summed over 24 hours
MC iterations = 100; MC list in residue file; MC seed = 1; RNG = MS VB
Run Comment: "Dose in ug/kg/day, Residue in ppb"
==========

Children 6-12

2-Day Avg Exposure Analysis
(mg/kg body-weight/day)

	per Capita	per User
Mean	0.002060	0.002060
Standard Deviation	0.002166	0.002166
Margin of Exposure	12,138	12,138
Percent of aRfD	0.82	0.82

Percent of Individuals that are Users (over two days) = 100.00%

Estimated percentile of user-days falling below calculated exposure in mg/kg body-wt/day with Margin of Exposure (MOE) and Percent of aRfD

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
10.00	0.000604	0.24	41,389	90.00	0.003671	1.47	6,809
20.00	0.000849	0.34	29,432	95.00	0.004765	1.91	5,246
30.00	0.001083	0.43	23,085	97.50	0.006373	2.55	3,923
40.00	0.001315	0.53	19,012	99.00	0.010049	4.02	2,487
50.00	0.001580	0.63	15,822	99.50	0.017465	6.99	1,431
60.00	0.001886	0.75	13,258	99.75	0.021064	8.43	1,186
70.00	0.002252	0.90	11,101	99.90	0.026499	10.60	943
80.00	0.002743	1.10	9,113				

Estimated percentile of per-capita days falling below calculated exposure in mg/kg body-wt/day with Margin of Exposure (MOE) and Percent of aRfD

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
10.00	0.000604	0.24	41,389	90.00	0.003671	1.47	6,809
20.00	0.000849	0.34	29,432	95.00	0.004765	1.91	5,246
30.00	0.001083	0.43	23,085	97.50	0.006373	2.55	3,923
40.00	0.001315	0.53	19,012	99.00	0.010049	4.02	2,487
50.00	0.001580	0.63	15,822	99.50	0.017465	6.99	1,431
60.00	0.001886	0.75	13,258	99.75	0.021064	8.43	1,186
70.00	0.002252	0.90	11,101	99.90	0.026499	10.60	943
80.00	0.002743	1.10	9,113				

Residue file: Dicrotophos acute food+water ppb.R10
Adjustment factor #2 NOT used.
Analysis Date: 12-14-2016/15:54:04 Residue file dated: 12-14-2016/09:05:28
NOEL (Acute) = 25.000000 mg/kg body-wt/day
Acute Reference Dose (aRfD) = 0.250000 mg/kg body-wt/day
Two-Day Average Results Reported
RAC/FF intake summed over 24 hours
MC iterations = 100; MC list in residue file; MC seed = 1; RNG = MS VB
Run Comment: "Dose in ug/kg/day, Residue in ppb"
==========

Youth 13-19

2-Day Avg Exposure Analysis
(mg/kg body-weight/day)

	per Capita	per User
Mean	0.001283	0.001283
Standard Deviation	0.001335	0.001335
Margin of Exposure	19,480	19,480
Percent of aRfD	0.51	0.51

Percent of Individuals that are Users (over two days) = 100.00%

Estimated percentile of user-days falling below calculated exposure in mg/kg body-wt/day with Margin of Exposure (MOE) and Percent of aRfD

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
10.00	0.000350	0.14	71,440	90.00	0.002401	0.96	10,412
20.00	0.000501	0.20	49,945	95.00	0.003101	1.24	8,060
30.00	0.000656	0.26	38,131	97.50	0.003965	1.59	6,304
40.00	0.000839	0.34	29,810	99.00	0.006291	2.52	3,973
50.00	0.001008	0.40	24,810	99.50	0.009585	3.83	2,608
60.00	0.001173	0.47	21,309	99.75	0.010258	4.10	2,437
70.00	0.001404	0.56	17,802	99.90	0.016051	6.42	1,557
80.00	0.001701	0.68	14,694				

Estimated percentile of per-capita days falling below calculated exposure in mg/kg body-wt/day with Margin of Exposure (MOE) and Percent of aRfD

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
10.00	0.000350	0.14	71,440	90.00	0.002401	0.96	10,412
20.00	0.000501	0.20	49,945	95.00	0.003101	1.24	8,060
30.00	0.000656	0.26	38,131	97.50	0.003965	1.59	6,304
40.00	0.000839	0.34	29,810	99.00	0.006291	2.52	3,973
50.00	0.001008	0.40	24,810	99.50	0.009585	3.83	2,608
60.00	0.001173	0.47	21,309	99.75	0.010258	4.10	2,437
70.00	0.001404	0.56	17,802	99.90	0.016051	6.42	1,557
80.00	0.001701	0.68	14,694				

Residue file: Dicrotophos acute food+water ppb.R10
Adjustment factor #2 NOT used.
Analysis Date: 12-14-2016/15:54:04 Residue file dated: 12-14-2016/09:05:28
NOEL (Acute) = 25.000000 mg/kg body-wt/day
Acute Reference Dose (aRfD) = 0.250000 mg/kg body-wt/day
Two-Day Average Results Reported
RAC/FF intake summed over 24 hours
MC iterations = 100; MC list in residue file; MC seed = 1; RNG = MS VB
Run Comment: "Dose in ug/kg/day, Residue in ppb"
==========

Adults 20-49

	2-Day Avg Exposure Analysis (mg/kg body-weight/day) per Capita	per User
Mean	0.000933	0.000933
Standard Deviation	0.001006	0.001006
Margin of Exposure	26,795	26,795
Percent of aRfD	0.37	0.37

Percent of Individuals that are Users (over two days) = 100.00%

Estimated percentile of user-days falling below calculated exposure in mg/kg body-wt/day with Margin of Exposure (MOE) and Percent of aRfD

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
10.00	0.000265	0.11	94,436	90.00	0.001662	0.66	15,046
20.00	0.000397	0.16	63,040	95.00	0.002156	0.86	11,594
30.00	0.000509	0.20	49,147	97.50	0.002704	1.08	9,244
40.00	0.000619	0.25	40,356	99.00	0.003913	1.57	6,388
50.00	0.000735	0.29	34,003	99.50	0.005836	2.33	4,283
60.00	0.000877	0.35	28,497	99.75	0.009790	3.92	2,553
70.00	0.001036	0.41	24,123	99.90	0.013102	5.24	1,908
80.00	0.001276	0.51	19,589				

Estimated percentile of per-capita days falling below calculated exposure in mg/kg body-wt/day with Margin of Exposure (MOE) and Percent of aRfD

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
10.00	0.000265	0.11	94,436	90.00	0.001662	0.66	15,046
20.00	0.000397	0.16	63,040	95.00	0.002156	0.86	11,594
30.00	0.000509	0.20	49,147	97.50	0.002704	1.08	9,244
40.00	0.000619	0.25	40,356	99.00	0.003913	1.57	6,388
50.00	0.000735	0.29	34,003	99.50	0.005836	2.33	4,283
60.00	0.000877	0.35	28,497	99.75	0.009790	3.92	2,553
70.00	0.001036	0.41	24,123	99.90	0.013102	5.24	1,908
80.00	0.001276	0.51	19,589				

Residue file: Dicrotophos acute food+water ppb.R10
Adjustment factor #2 NOT used.
Analysis Date: 12-14-2016/15:54:04 Residue file dated: 12-14-2016/09:05:28
NOEL (Acute) = 25.000000 mg/kg body-wt/day
Acute Reference Dose (aRfD) = 0.250000 mg/kg body-wt/day
Two-Day Average Results Reported
RAC/FF intake summed over 24 hours
MC iterations = 100; MC list in residue file; MC seed = 1; RNG = MS VB
Run Comment: "Dose in ug/kg/day, Residue in ppb"
==========

Adults 50-99

2-Day Avg Exposure Analysis
(mg/kg body-weight/day)

	per Capita	per User
Mean	0.000726	0.000726
Standard Deviation	0.000602	0.000602
Margin of Exposure	34,416	34,416
Percent of aRfD	0.29	0.29

Percent of Individuals that are Users (over two days) = 100.00%

Estimated percentile of user-days falling below calculated exposure in mg/kg body-wt/day with Margin of Exposure (MOE) and Percent of aRfD

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
10.00	0.000219	0.09	114,155	90.00	0.001369	0.55	18,262
20.00	0.000315	0.13	79,273	95.00	0.001737	0.69	14,392
30.00	0.000407	0.16	61,467	97.50	0.002087	0.83	11,979
40.00	0.000490	0.20	50,971	99.00	0.002860	1.14	8,741
50.00	0.000588	0.24	42,551	99.50	0.003639	1.46	6,870
60.00	0.000691	0.28	36,184	99.75	0.004263	1.71	5,864
70.00	0.000830	0.33	30,132	99.90	0.006868	2.75	3,640
80.00	0.001020	0.41	24,506				

Estimated percentile of per-capita days falling below calculated exposure in mg/kg body-wt/day with Margin of Exposure (MOE) and Percent of aRfD

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
10.00	0.000219	0.09	114,155	90.00	0.001369	0.55	18,262
20.00	0.000315	0.13	79,273	95.00	0.001737	0.69	14,392
30.00	0.000407	0.16	61,467	97.50	0.002087	0.83	11,979
40.00	0.000490	0.20	50,971	99.00	0.002860	1.14	8,741
50.00	0.000588	0.24	42,551	99.50	0.003639	1.46	6,870
60.00	0.000691	0.28	36,184	99.75	0.004263	1.71	5,864
70.00	0.000830	0.33	30,132	99.90	0.006868	2.75	3,640
80.00	0.001020	0.41	24,506				

Residue file: Dicrotophos acute food+water ppb.R10
Adjustment factor #2 NOT used.
Analysis Date: 12-14-2016/15:54:04 Residue file dated: 12-14-2016/09:05:28
NOEL (Acute) = 25.000000 mg/kg body-wt/day
Acute Reference Dose (aRfD) = 0.250000 mg/kg body-wt/day
Two-Day Average Results Reported
RAC/FF intake summed over 24 hours
MC iterations = 100; MC list in residue file; MC seed = 1; RNG = MS VB
Run Comment: "Dose in ug/kg/day, Residue in ppb"
==========

Female 13-49

	2-Day Avg Exposure Analysis (mg/kg body-weight/day) per Capita	per User
Mean	0.000906	0.000906
Standard Deviation	0.000923	0.000923
Margin of Exposure	27,589	27,589
Percent of aRfD	0.36	0.36

Percent of Individuals that are Users (over two days) = 100.00%

Estimated percentile of user-days falling below calculated exposure in mg/kg body-wt/day with Margin of Exposure (MOE) and Percent of aRfD

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
10.00	0.000250	0.10	100,080	90.00	0.001645	0.66	15,200
20.00	0.000380	0.15	65,825	95.00	0.002174	0.87	11,497
30.00	0.000489	0.20	51,157	97.50	0.002844	1.14	8,790
40.00	0.000595	0.24	42,044	99.00	0.003859	1.54	6,478
50.00	0.000708	0.28	35,287	99.50	0.005006	2.00	4,994
60.00	0.000855	0.34	29,255	99.75	0.006721	2.69	3,719
70.00	0.001023	0.41	24,426	99.90	0.012175	4.87	2,053
80.00	0.001244	0.50	20,096				

Estimated percentile of per-capita days falling below calculated exposure in mg/kg body-wt/day with Margin of Exposure (MOE) and Percent of aRfD

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
10.00	0.000250	0.10	100,080	90.00	0.001645	0.66	15,200
20.00	0.000380	0.15	65,825	95.00	0.002174	0.87	11,497
30.00	0.000489	0.20	51,157	97.50	0.002844	1.14	8,790
40.00	0.000595	0.24	42,044	99.00	0.003859	1.54	6,478
50.00	0.000708	0.28	35,287	99.50	0.005006	2.00	4,994
60.00	0.000855	0.34	29,255	99.75	0.006721	2.69	3,719
70.00	0.001023	0.41	24,426	99.90	0.012175	4.87	2,053
80.00	0.001244	0.50	20,096				

Ver. 4.02, 05-10-c
DEEM-FCID ACUTE Analysis for DICROTOPHOS NHANES 2005-2010 2-Day
Residue file: Dicrotophos acute food+water ppb.R10
Adjustment factor #2 NOT used.
Analysis Date: 12-14-2016/15:54:04 Residue file dated: 12-14-2016/09:05:28
NOEL (Acute) = 25.000000 mg/kg body-wt/day
Acute Reference Dose (aRfD) = 0.250000 mg/kg body-wt/day
Two-Day Average Results Reported
RAC/FF intake summed over 24 hours
MC iterations = 100; MC list in residue file; MC seed = 1; RNG = MS VB
Run Comment: "Dose in ug/kg/day, Residue in ppb"
==========

Custom demographics 1: Adults, 18+ yrs
Sex: M/F-all/
All Races
Age-Low: 18 yrs High: 99 yrs

	2-Day Avg Exposure Analysis (mg/kg body-weight/day) per Capita	per User
Mean	0.000858	0.000858
Standard Deviation	0.000878	0.000878
Margin of Exposure	29,138	29,138
Percent of aRfD	0.34	0.34

Percent of Individuals that are Users (over two days) = 100.00%

Estimated percentile of user-days falling below calculated exposure in mg/kg body-wt/day with Margin of Exposure (MOE) and Percent of aRfD

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
10.00	0.000244	0.10	102,648	90.00	0.001583	0.63	15,793
20.00	0.000362	0.14	69,125	95.00	0.002016	0.81	12,398
30.00	0.000461	0.18	54,174	97.50	0.002550	1.02	9,802
40.00	0.000566	0.23	44,182	99.00	0.003608	1.44	6,929
50.00	0.000672	0.27	37,184	99.50	0.004735	1.89	5,279
60.00	0.000803	0.32	31,129	99.75	0.007819	3.13	3,197
70.00	0.000962	0.38	25,998	99.90	0.010661	4.26	2,344
80.00	0.001189	0.48	21,022				

Estimated percentile of per-capita days falling below calculated exposure in mg/kg body-wt/day with Margin of Exposure (MOE) and Percent of aRfD

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
10.00	0.000244	0.10	102,648	90.00	0.001583	0.63	15,793
20.00	0.000362	0.14	69,125	95.00	0.002016	0.81	12,398
30.00	0.000461	0.18	54,174	97.50	0.002550	1.02	9,802
40.00	0.000566	0.23	44,182	99.00	0.003608	1.44	6,929
50.00	0.000672	0.27	37,184	99.50	0.004735	1.89	5,279
60.00	0.000803	0.32	31,129	99.75	0.007819	3.13	3,197
70.00	0.000962	0.38	25,998	99.90	0.010661	4.26	2,344
80.00	0.001189	0.48	21,022				

Appendix V. Human Exposure Assessment for Dicrotophos Used on Cotton

December 8, 2016

Special Local Needs (24c) Label Review:
Human Exposure Assessment
For Dicrotophos used on Cotton

Mai Ngo, Ph.D.

Eric Kwok, Ph.D. D.A.B.T.

Terri Barry, Ph.D.

Human Health Assessment Branch

California Department of Pesticide Regulation

INTRODUCTION

Dicrotophos, dimethyl phosphate of 3-hydroxy N,N-dimethyl-cis-crotonamide, is an organophosphate (OP) pesticide with broad spectrum insecticidal activity. Currently, there are no dicrotophos products registered for use in the State of California. This exposure assessment is to address potential human exposures resulting from use of BIDRIN® 8, a water miscible formulation consisting of 82% dicrotophos, as part the review process for a FIFRA section 24(c) Special Local Need (SLN) label registration. This exposure assessment, completed by the Human Health Assessment Branch (HHA) of the California Department of Pesticide Regulation (DPR) will consider use on cotton plants for the control of brown stink bug within the State of California.

PHYSIOCHEMICAL PROPERTIES

Dicrotophos is a yellow to brown liquid with a mild, ester odor (generally described as a fruity or pleasant odor) (TOXNET, 2016). Dicrotophos is classified as a moderately persistent systemic insecticide and acaricide, and dicrotophos is a mixture of the E- and Z-isomers. The commercial grade consists of 85% E-isomer, which is the pesticidally active isomer of the two. The physiochemical properties and other reference information for dicrotophos are listed in Table 1.

Chemical Structure [b]:

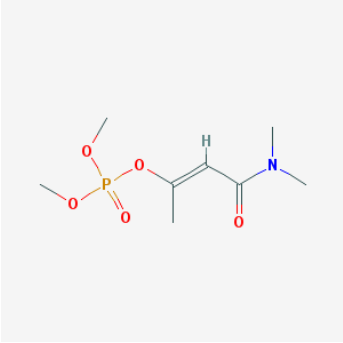

Table 1. Physicochemical Properties of Dicrotophos.

Manufacturer	Amvac Chemical Corporation, 4100 E. Washington Blvd., Los Angeles, CA 30023
24(c) Registrant	California Cotton Ginners and Growers Association, 1785 N. Fine Avenue, Fresno, CA 93727
EPA Reg No.	5481-448
DPR Chem Code	72
EPA PC Code	035201
MRID No.	45099501, 45099502, 46484501
CAS number [b]	141-66-2; 3725-78-2 for the mined isomers; 141-66-2 for the E-isomer; 18250-63-0 for the Z-isomer
Physical appearance [b]	the pure material forms a yellow to brown liquid with a mild ester-like odor
Chemical name [b]	dimethyl (E)-2-dimethylcarbamoyl-1-methylvinyl phosphate; 3-dimethoxyphosphinyloxy-N, N-dimethylisocrotonamide; E-isomer of O,O-dimethyl-O-(3-dimethylamino-1-methyl-3-oxo-1-propenyl) phosphate; 2-Dimethyl-cis-2-dimethylcarbamoyl-1-methylvinylphosphate
Trade names [b]	Bidrin, Carbicron, Diapadrin, Dicron, Ektafos
Molecular formula [a]	$C_8H_{16}NO_5P$
Molecular weight [b]	237.21 g/mol
Solubility [b]	Miscible with water; miscible with acetone, alcohol,

Solubility continued	acetonitrile, chloroform, methylene chloride, and xylene. Barely soluble in mineral oils. Slightly soluble in kerosene and diesel fuel (<1%)
Flashpoint [b]	> 200°F
Melting point [b]	<25°C
Boiling point [c, d]	725°F; 400 °C at 760 mm Hg; 130 °C at 0.1 mm Hg
Vapor pressure [b, d]	9.3 mPa at 20° C; technical, 1×10^{-4} mmHg at 20° C; Pure, 6.98×10^{-5} mmHg at 20°C; 21.3 mPa at 25 °C; 1.60×10^{-4} mm Hg at 25 °C
Henry's Law constant [d]	9.06×10^{-10} (dimensionless) at 20 °C 5.1×10^{-6} Pa m^3/mol at 25 °C 5.03×10^{-11} atm m^3/mol at 25 °C
Relative density/ Specific gravity [a, d]	1.22 g/cm^3 at 15 °C
Log K_{oc} [b]	1.04 – 2.27
Log K_{ow} [a, d]	-0.49; 0.00

[a] (http://pubchem.ncbi.nlm.nih.gov); [b] (www.extoxnet.orst.edu); [c] (www.cdc.gov);
[d] (https://toxnet.nlm.nih.gov)

TOXICITY

Like all OP pesticides, the mode-of-action of dicrotophos involves inhibition of the enzyme, acetylcholinesterase (AChE), which leads to accumulation of acetylcholine and ultimately to neurotoxicity in the central and/or peripheral nervous system.

Unlike some OPs, which require transformation to their oxon metabolites, dicrotophos exhibits AChE-inhibiting activity directly. Absorption and distribution are rapid in rats, with extensive metabolism (and detoxification), and no tissue accumulation (U.S. EPA, 2015a). However, a small amount (3%) of dicrotophos is converted to monocrotophos *in vivo*, which also exhibits the same AChE-inhibiting activity as its parent compound.

Exposure to dicrotophos may occur through dermal contact and inhalation in the occupational setting. Exposure may also occur in the residential setting from spray drift and take-home dust. The general population may also be exposed by ingestion of food with dicrotophos residue (TOXNET, 2016).

ENVIRONMENTAL FATE

Dicrotophos is rapidly degraded under aerobic and anaerobic conditions to form N,N-dimethylbutyramide (a major product of hydrolytic degradation), carbon dioxide, and other

minor degradation products. The hydrolysis of dicrotophos in soil and water appears to be pH-dependent with the half-life of dicrotophos being 117, 72, and 28 days in buffer solutions of pH 5, 7, and 9, respectively (EXTOXNET, 1998).

Soil mobility is expected to be moderate to very high and degradation products do not persist in the environment (EXTOXNET, 1998; TOXNET, 2016). In soil, the dimethylamino group first converts to an N-oxide and then to a hydroxymethyl and aldehyde groups, followed by demethylation and hydrolysis (EXTOXNET, 1998).

Absorption to suspended solids and sediment is predicted by the K_{oc} values (TOXNET, 2016). However, Henry's Law constant does not support volatilization from water surfaces. In the aqueous environment, decomposition of dicrotophos is generally expected to be by hydrolysis.

Dicrotophos can exist in both the vapor and particulate phase in the atmosphere. The vapors are subject to photochemical degradation and photolysis, with the particulate-phase being removed by wet and dry deposition (TOXNET, 2016).

U.S. EPA STATUS

Dicrotophos is federally classified as a "Restricted Use Pesticide" product and may be purchased and used only by certified applicators or persons under their direct supervision. U.S. EPA completed and revised a human health risk assessment for registration review to support currently registered uses of dicrotophos (U.S. EPA, 2014; 2015b). Only a water-miscible formulation of dicrotophos for foliar application to established cotton plants or use as a micro-injection treatment for ornamental and non-food producing trees is currently registered for use with U.S. EPA.

USAGE

The warm springs, hot summers, and dry falls of the California San Joaquin Valley, Palo Verde Valley of Southern California, and Sacramento Valley provide the long growing season required by cotton (CCGGA, 2014). American Pima cotton appears to be the prominent type of cotton grown in California (CottonJourney.com, 2015). California cotton production varies year to year. Planted in March and April, cotton is commonly furrow irrigated, and sometimes border-strip or sprinkler irrigated in California. Drip irrigation is also becoming more prevalent in recent years. By eight weeks after planting the first flower buds form, after which blooming soon follows. Once irrigation ceases in August (16-18 weeks from planting), the plant is allowed to dry out; the crop is then mechanically harvested. According to USDA (2010), "usual harvesting dates" for cotton in California begin October 5 and end November 20. It normally takes four to seven months (25 weeks) from planting to harvest, depending on the species of cotton grown (USDA, 2010; CottonJourney.com, 2015; GardeningKnowHow.com, 2015). In

addition to the cotton fibers, cottonseed is pressed into oil for cooking and cosmetics (CCGGA, 2014). The cottonseed hulls are primarily used as livestock feed.

Dicrotophos is a federal registered "restricted use" pesticide intended for closed-system delivery to cotton fields via aerial and ground equipment. The proposed 24(c) SLN product label indicates late season use, from first bloom to 30 days prior to harvest, for the control of the brown stink bug in Imperial, Riverside, and San Bernardino Counties. The application guidelines on the proposed label are summarized in Table 2.

Table 2. Summary of Directions for Use of Dicrotophos on Cotton.

Application timing, type, and equipment	Late season use (first bloom to 30 days prior to harvest); Air or ground application. No chemigation/application through any type of irrigation system.
Formulation	Water-miscible formula for foliar application or as micro- injection treatment.
Application rate	4.0 - 8.0 (fl oz/acre) OR 0.25 - 0.5 (lbs/acre)
Max. applications per season	Minimum interval between applications is 14 days. No more than 16 fl. oz/acre (1 lb AI/acre) during "growth period" (late season).
REI (days)	6
PHI (days)	30
Use directions and limitations	Locations for use are Imperial, Riverside, and San Bernardino counties. Dicrotophos is both Federally-Restricted and California Restricted material (A restricted materials permit must be obtained from CACs before use).

The proposed 24(c) SLN label indicates use on cotton with a maximum single application rate of 0.5 lbs AI/acre via ground or aerial application, specified to be conducted by closed-system only, with a pre-harvest interval (PHI) of 30 days. Since the minimum application interval is 14 days and the use of this product is being limited to 1 lb/acre "during this growth period," HHA

assumes a maximum of two applications in a seasonal exposure period of approximately 3 months. There are currently no registered uses for dicrotophos in the State of California.

A query of California's Pesticide Use and Reporting (PUR) program showed that dicrotophos was rarely used within the most recent 10 years in California. One application was reported in 2005 and two were reported in 2006. Available application details are provided in Table 3.

Table 3. Previous Use of Dicrotophos in California.

Year	Month	County	Site	Product	Amount applied (lbs)	Acres treated	Application method
2005	6	Riverside	Landscape	INJECT-A-CIDE B	2.0	-	-
2006	1	Colusa	Alfalfa	RED-TOP BIDRIN INSECTICIDE	5.2	110	Ground
2006	11	Calaveras	Rights of way	DU PONT BIDRIN 8 WATER MISCIBLE INSECTICIDE	1.1	-	-

FORMULATION

The proposed 24(c) SLN is for BIDRIN® 8, a water miscible formulation containing 82% active ingredient, dicrotophos, or 8 lbs active ingredient per gallon.

LABEL PRECAUTIONS

Precautionary Statements

- DANGER, POISON, PLEIGRO, Keep out of Reach of Children, with skull and crossbones symbol
- Hazards to humans and domestic animals.
- DANGER: fatal if swallowed. May be fatal if absorbed through skin or if inhaled. Causes moderate eye irritation. Do not get in eyes, on skin, or on clothing. Do not breathe spray mist. Prolonged or frequently repeated skin contact may cause allergic reactions in some individuals.
- Combustible: Do not use or store near heat or open flame.

Personal Protective Equipment (PPE) Requirements

- **Personal protective equipment (PPE)**:
    - chemical-resistant materials for this product include barrier laminate, butyl rubber, nitrile rubber, neoprene rubber, PVC, or viton, or category C on EPA chemical-resistance category selection chart.
    - When specified, a respirator with an organic-vapor removing cartridge with a particulate prefilter approved for pesticides (NIOSH approval number prefix TC-23C), or a canister approved for pesticides (NIOSH approval number prefix TC-14G), or a NIOSH approved respirator with an organic vapor (OV) cartridge or canister with any N, R, or HE prefilter.
- **Mixers/loaders/applicators and other handlers using engineering controls** must wear:
    - long-sleeve shirt and long pants
    - chemical resistant footwear plus socks
    - "Engineering Controls", listed below, as additional requirements
- **Engineering Controls:**
    - **Mixers/loaders must use a closed system** that meets the requirements listed in the WPS for agricultural pesticides, for providing dermal and inhalation protection.
        - In addition, **mixers/loaders using engineering controls** must wear:
            - chemical-resistant gloves
            - chemical-resistant apron
            - wear protective eyewear
            - wear PPE required in the PPE section for mixers/loaders using engineering controls
        - In addition, **mixers/loaders** must be provided/have immediately available/must use **in an emergency** (such as spill or equipment breakdown) the following:
            - coveralls
            - chemical-resistant footwear
            - respirator with an organic-vapor removing cartridge with a prefilter approved for pesticides, or a canister approved for pesticides, or a NIOSH approved respirator with an organic vapor (OV) cartridge or canister with any N, R, or HE prefilter.
    - **Applicators** using motorized ground equipment must use an enclosed cab that meets WPS for Agricultural Pesticides (40 CFR) for dermal protection.
        - **Pilots** must use an enclosed cockpit in a manner that meets requirements listed in WPS for agricultural pesticides [40 CFR Part 170.240 (d)(6)]
        - In addition, **applicators** must:

        - Wear PPE required in PPE section for applicators using engineering controls.
        - Either wear the type of respirator specified for PPE, or use an enclosed cab that provides at least as much respirator protection as the type of respirator specified, or use an enclosed cab as defined in Title 3, California Code of Regulations (3 CCR, Section 6000) under enclosed cab acceptable for respiratory protection.
    - Applicators must be provided/have immediately available for use, and must use **in an emergency** when they exit the cab in the treated area:
        - Coveralls
        - Chemical-resistant gloves
        - Chemical-resistant footwear
        - Chemical-resistant headgear
    - If overhead exposure, and if using an enclosed cab that provides respiratory protection, a respirator of the type specified on label.
- **Handlers performing tasks for which engineering controls are not feasible**, such as spill clean-up or equipment cleaning, must wear, IN ADDITION to the PPE specified above for mixers and loaders:
    - coveralls, chemical-resistant footwear plus socks
    - respirator which meets above-mentioned requirements of label
- **PPE required for early entry to treated areas** that is permitted under the WPS and that involves contact with anything that has been treated, such as plants, soil, or water is:
    - coveralls worn over long-sleeve shirt and long pants
    - chemical-resistant gloves made of any waterproof material
    - chemical-resistant footwear plus socks
    - protective eyewear
    - chemical-resistant headgear for overhead exposure

<u>User Safety Requirements and Engineering Controls</u>

- **Cleaning and maintenance of PPE** following manufacturer's instructions. If no such instructions for washables exist, use detergent and hot water. Keep and wash PPE separately from other laundry. Discard clothing and other absorbent materials that have been drenched or heavily contaminated with this product's concentrate. Do not reuse them.
- **Engineering controls:** Mixers/loaders must use a closed system that meets the requirements listed in the WPS for agricultural pesticides, for providing dermal and inhalation protection. In addition, mixers/loaders must wear PPE required in the PPE section for mixers/loaders using engineering controls, wear protective eyewear, be provided/have immediately available/must use in an emergency (such as spill or

equipment breakdown) the following: coveralls, chemical-resistant footwear, respirator with an organic-vapor removing cartridge with a prefilter approved for pesticides, or a canister approved for pesticides, or a NIOSH approved respirator with an organic vapor (OV) cartridge or canister with any N, R, or HE prefilter.

- **Applicators using motorized ground equipment must use an enclosed cab** that meets the definition in the Worker Protection Standard (WPS) for Agricultural Pesticides [40 CFR Part 170.240(d)(5)] for dermal protection. In addition, such applicators must wear PPE required in the PPE section for applicators using engineering controls, wear the type of respirator specified on label or use an enclosed cab that provides at least as much respirator protection as the specified respirator, or use an enclosed cab as defined in Title 3, California Code of Regulations, section 6000 (3 CCR section 6000) under enclosed cab acceptable for respiratory protection. Coveralls, chemical-resistant gloves, chemical-resistant footwear, chemical-resistant headgear must be made immediately available for use upon exiting the cab in an emergency. If using an enclosed cab that provides respiratory protection, a respirator of specified type must also be made available.
- **Wash hands** before eating, drinking, chewing gum, using tobacco, or using the toilet. Remove clothing/PPE immediately if pesticide gets inside, then wash thoroughly and replace with clean clothing. Remove PPE immediately after handling product and wash thoroughly and change into clean clothing.
- **Some certified crop advisors, and persons performing crop advising tasks** under their direct supervision, may be exempt from certain provisions of the WPS [40 CFR Part 170], as specified in the WPS at 40 CFR Part 170.104(b) and 170.204(b).

Directions for Application

- Use this product only in accordance with its labeling and with the Worker Protection Standard [40 CFR Part 170].
- Do not apply this product through any type of irrigation system.
- Do not allow this product to drift. The applicator also must use all other measures necessary to control drift.
- Do not enter or allow worker entry into the treated areas during the restricted-entry interval (REI) of 6 days.
- Notify workers of the application by warning them orally and by posting warning signs at the entrances to treated areas.
- This product is both Federally-restricted and California-restricted. A restricted materials permit must be obtained from the county agricultural commissioner prior to this use.
- Do not use in mixture with other pesticides unless provided for in the labeling. Trial on a small area to check out unanticipated problems is suggested.
- Do not contaminate water, food, or feed by storage or disposal.

ILLNESS AND INJURY REPORTS

A Pesticide Illness/Injury Query (CalPIQ) was made from the year of the database was established to the most recently available data (1992 to 2012). The query resulted in only one case, reported for 2008. The relationship of illness to dicrotophos and another OP pesticide, terbufos, was defined as probable. The patient was a chemist of a chemical manufacturer in Los Angeles County. He worked with OP pesticides in the lab but didn't describe how he was exposed to the chemical. Cholinergic symptoms were seen but cholinesterase activities were said to be normal. The patient was hospitalized for 5 days and was treated with atropine and 2-PAM (also called pralidoxime**).**

U.S. EPA reviewed data for human incidents of dicrotophos-related illness (U.S. EPA, 2012a). Most notably, analysis of the National Institute of Occupational Safety and Health Sentinel Event Notification System for Occupational Risks (NIOSH SENSOR) from 1998 to 2008 identified 26 cases (or individuals) of dicrotophos exposure. In summary, 17 of these 26 cases were classified as minor severity, 4 as moderate severity, and 5 as high severity. Sixteen of the 26 cases were work-related. There was one case of residential exposure involved a child coming in contact with a product container. The remaining 9 cases were bystander exposures to spray drift from aerial applications to cotton, a scenario of concern for this exposure assessment.

DERMAL ABSORPTION

A 28-day rat toxicity study of dicrotophos (Noakes, 2004) is the basis of U.S. EPA's risk assessment. U.S. EPA used the steady-state dermal and inhalation Points of Departures (PoD) based on route-specific toxicity studies, and therefore, no absorption factors were deemed necessary to estimate absorbed dose. However, the Agency did multiply the PoD derived from the 28-day dermal rat toxicity study (PoD = 2.1 mg/kg/day) by a factor of 4.44 to account for a higher skin permeability in rats.

U.S. EPA evaluated one *in vivo* dermal penetration rat study (Gledhill, 1999) and one *in vitro* human and rat epidermis absorption study (Davies, 1999) for dicrotophos (U.S. EPA, 2015b). Briefly, *in vivo* absorption from the rat studies ranged from 32.9% (4 $\mu g/cm^2$) to 34.9% (40 ug/cm^2 dose), while *in vitro* absorption from the rat studies ranged from 47.1% (4 $\mu g/cm^2$) to 57.7% (40 ug/cm^2 dose). *In vitro* absorption from the human study found 10.6 % and 12.2% absorption from a dose of 4 $\mu g/cm^2$ and 40 $\mu g/cm^2$, respectively.

HHA found Gledhill (1999) to be of high quality with reliable data. However, less confidence can be placed on the results from Davis (1999) due to absence of data points and incomplete or inconsistent procedural and technical information. Neither anatomical region nor gender was indicated for human skin samples. In addition, the authors did not indicate how samples were retrieved or stored prior to preparation and eventual freezing. Because the Davis study was

completed in 1999, it does not meet current requirements of demonstrating adequate solubility of the test compound in the receptor fluid and providing the results for a relevant reference chemical run concurrently with the test substance (OECD, 2004). In addition, there appears to be a higher level of variability in the data values, with total recovery ranging from 79.9% to 132% throughout the study. For the lowest dose of 9.66 $\mu g/cm^2$, total recovery at 24 hours post-application ranged from 117% to 132% for the human tissue samples, with an average percent recovery of 124.7%. These high recovery values (i.e., > 110%) reduce the amount of confidence that can be placed on this study. One strength of the study is that both animal and human samples were evaluated concurrently under the same experimental protocols. The use of the same test conditions is a fundamental principle in the "triple-pack" methodology, as *in vitro* test variables are recognized to greatly influence the test outcome.

TRIPLE-PACK APPROACH TO DERMAL ABSORPTION

HHA policy is to use chemical-specific data when available, and surrogate data or default values when high quality chemical-specific data are not available. Since *in vivo* human data is rarely available, it is often necessary to utilize animal studies, with increasing reliance upon *in vitro* data.

In vitro data is highly variable, influenced by numerous experimental factors such as receptor fluid composition, diffusion cell type, and skin sample preparation. An inter-laboratory study comparing the *in vitro* absorption values for caffeine, testosterone, and benzoic acid found relatively high standard deviation values for mean absorption when averaged across the 10 independent laboratories, even though the same protocol and OECD guidance was provided (van de Sandt *et al.*, 2004). Although relatively detailed, the experimental protocols did not define all possible variables. Study parameters such as sample thickness, body site, diffusion cell type, and receptor compartment volumes were not defined. One of the ten laboratories utilized animal skin, rather than human skin. All laboratories ranked benzoic acid as having the highest absorption; however, only seven of the nine laboratories utilizing human skin determined the absorption of caffeine to be higher than testosterone. Even with efforts made to standardize study protocol, this study emphasizes the impact of experimental variables on the results from dermal absorption studies. Consistent and detailed experimental guidelines must be followed for an *in vitro* study to be comparable to another. Requiring the same test conditions are used with both the animal and human *in vitro* studies helps to increase predictability and make comparisons between studies appropriate.

For the purpose of this SLN product review for BIDRIN® 8, the registrant-submitted dermal absorption studies were evaluated using the "triple-pack" criteria (Ngo, 2015 and Appendix III). Briefly, the "triple-pack" approach correlates *in vitro* and *in vivo* animal and *in vitro* human data to make references about an appropriate human dermal absorption factor value for human health risk assessment. Relating the *in vitro* to *in vivo* dermal absorption of a compound from experimental animal studies is one approach to corroborate *in vitro* data. If the ratio of the *in*

vitro to *in vivo* animal data approaches the value of one, with the "triple-pack" method, it may infer that the *in vitro* test conditions were an appropriate simulation of *in vivo* absorption process (NAFTA TWA, 2008). This method of using the "triple-pack" is based on the assertion that *in vitro* data alone is unreliable for the determination of a human DAF, and has been utilized by both U.S. EPA (2008; 2010; 2013a) and PMRA (2011; 2015), two of the main developers of this approach. Secondly, if the *in vitro* test conditions were proven to be "appropriate" and these same test conditions were used to generate absorption data in human skin, there could be greater confidence that those results are dependable for evaluating *in vivo* human absorption. This method of using the triple pack is based on the assertion that *in vitro* data alone is unreliable for the determination of human dermal absorption, and has been utilized by both U.S. EPA (2008; 2010; 2013a) and PMRA (2011; 2015), two of the main developers of this approach.

In this assessment, the registrant-submitted *in vitro* dermal absorption studies were determined to be suitable for estimating dermal absorption. The ratio of *in vitro* animal data to *in vivo* animal data is used to determine the reliability of the *in vitro* test conditions to predict *in vivo* absorption. Data quality and variability is incorporated into the triple-pack analysis by calculating the 95th percentile confidence interval (CI) of the ratios. In our analysis for dicrotophos, the 95th percentile CI was estimated to be 0.88-1.59. Using the upper value of the 95th percentile CI, the calculated dermal absorption value of 26.3% was used for human health exposure and risk estimates for BIDRIN® 8 (Ngo, 2015).

It is important to note that the triple-pack-derived value of 26.3% is supported by a human dermal penetration study of monocrotophos, a metabolite and analogue of dicrotophos (Feldmann and Maibach, 1974). Monocrotophos is another OP insecticide with very similar physiochemical properties to dicrotophos. In the study, 12 pesticides including monocrotophos (azodrin) were applied to the forearms of human subjects at a dose of 4 $\mu g/cm^2$. Urinary elimination of monocrotophos was determined following intravenous administration to correct for incomplete urinary excretion. Once corrected for incomplete urinary elimination, monocrotophos absorption was 14.7 ± 7.1% of the administered dose. Assuming a normal distribution of the data, the 95th percentile estimate for human absorption of monocrotophos would be 26.4%.

HUMAN EXPOSURE

Based on the 24c SLN label-specified uses of dicrotophos, this exposure assessment evaluates only the acute and seasonal exposures in humans. Longer term exposures (i.e., annual/lifetime) are not anticipated. This assessment uses the maximum application rate of 0.5 lb/acre for Bidrin® 8 to estimate exposures. Default values for acreage treated or amount of pesticide handled under various scenarios are based on the ExpoSAC Policy 9.1 (U.S. EPA, 2001). In the

absence of adequate chemical-specific data, HHA assumes a default value of 100% in addressing the inhalation absorption of airborne pesticides (Frank, 2008).

Occupational Handler Exposure

Dicrotophos-specific data were not available for assessing exposure of individuals working as mixer/loader, applicator, or flagger. Exposure estimates for these exposure scenarios were derived using the Pesticide Handlers Exposure Database (PHED) (Versar, 1995). PHED was developed by U.S. EPA, Health Canada, and the American Crop Protection Association to provide non-chemical-specific (generic) pesticide handler exposure estimates for certain use scenarios. It contains monitoring data on dermal and inhalation exposures for handlers performing mixing, loading, application, and flagging tasks, primarily in support of agricultural pesticide applications. The database also combines exposure data from multiple field monitoring studies of different active ingredients. Subsets of the data may be selected for specific or similar application methods and formulation types to represent actual scenarios and active ingredients being evaluated. HHA uses estimates from PHED data subsets, selected for each scenario based upon certain criteria such as data quality, test material, and task specification, adjusted in accordance with HHA policy (Beauvais *et al.*, 2007). This exposure assessment also accounts for various protection factors conferred by PPE and engineering controls. PHED scenarios and some calculations are provided in the table footnotes, with additional information available in Appendix I.

HHA typically utilizes single-day exposure levels in estimating the potential risks associated with "short-term exposures" (seven days or less in duration) and a 95th percentile upper-bound estimate of short-term exposure for protecting individuals with above-average exposures to acutely toxic concentrations of pesticides (Frank, 2009b). HHA also uses the 90% upper confidence limit (UCL) on the 95th percentile value when using PHED surrogate data to estimate the short-term exposure, to account for the added uncertainty due to the PHED data quality. HHA uses the 90% UCL on the arithmetic mean of daily exposure to estimate seasonal exposure using PHED data.

To evaluate handler's exposures, the estimates were based on the use of closed mixing and loading systems as required by Title 3 CCR 6746 for liquid formations of toxicity category I pesticides. Also, this exposure assessment assumed that no gloves are worn during aerial application, ground applications, and flagging. This assumption is based on label only specifying glove use during mixer/loader activities. At a minimum, this is consistent with the U.S. EPA assumptions for the flagging scenario.

During aerial applications, the short-term (ST) exposure estimate for flaggers is the highest estimate, with a total absorbed daily dose (STADD) of 0.216 mg/kg/day. The mixer/loader scenario is the next highest short-term exposure (total STADD of 0.118 mg/kg/day), followed by

the applicators exposure estimate (total STADD of 0.0907 mg/kg/day) (Table 4). As shown in Table 4, the dermal route is the primary source of dicrotophos exposure for agricultural handlers. For seasonal exposures, a similar exposure pattern is observed, with the estimated seasonal average daily doses (SADD) of 0.0777 mg/kg/day, 0.0425 mg/kg/day, and 0.0326 mg/kg/day for the flagger, mixer/loader, and applicators, respectively.

For the ground boom applications, estimated STADDs are 0.0197 mg/kg/day for mixer/loaders and 8.03×10^{-3} mg/kg/day for applicators (Table 5). The seasonal exposures are 7.09×10^{-3} mg/kg/day for mixer/loaders and 2.89×10^{-3} mg/kg/day for applicators. Like the aerial exposure scenarios, the dermal route is the main source of exposure for these estimates.

Table 4. Exposure Rates and Short-Term and Seasonal Exposure Estimates for Workers Handling Dicrotophos in Support of Aerial Applications

Handler Task	Short-Term (µg/lb AI handled)		Long-Term (µg/lb AI handled)		STADD [d] (mg/kg/day)			SADD [e] (mg/kg/day)		
	Dermal	Inhalation	Dermal	Inhalation	Dermal	Inhalation	Total	Dermal	Inhalation	Total
M/L[a]	50.8	0.437	18.3	0.157	0.115	3.75×10^{-3}	0.118	0.0412	1.35×10^{-3}	0.0425
Applicator [b]	39.9	0.0916	14.3	0.0329	0.0899	7.85×10^{-4}	0.0907	0.0323	2.82×10^{-4}	0.0326
Flagger [c]	326.2	0.681	117.3	0.245	0.214	1.70×10^{-3}	0.216	0.0771	6.12×10^{-4}	0.0777

[a] Abbreviations: M/L = mixer/loader. M/Ls using engineering controls (ECs) are required to wear long-sleeved shirt and long pants, chemical resistant footwear and socks. ECs include task-specific PPE, protective eyewear, and use of a closed-system for removing and transfer of pesticide from shipping container to mixing tanks and/or application equipment. M/Ls using ECs are also required to use chemical-resistant gloves and chemical-resistant apron. M/Ls are required to use a closed system for removing and transfer of pesticide from shipping container to mixing tanks and/or application equipment. Estimates are based on scenario #6 from Beauvais *et al.* (2007) with additional protection factors of apron, chemical-resistant footwear, and eyewear, as detailed in Appendix I.

[b] Applicators using ECs are required to wear long-sleeved shirt and long pants, chemical resistant footwear and socks. Aerial applicators must use an enclosed cockpit which meets Worker Protection Standard (WPS) for agricultural pesticides. Use of gloves is not specified for applicator within the enclosed cockpit. Estimates are based on scenario #18 from Beauvais *et al.* (2007) with additional protection factors of chemical-resistant footwear, as detailed in Appendix I.

[c] No use of PPE, gloves, or ECs is specified for flagger. Estimates are based on scenario #7 from Beauvais *et al.* (2007), as detailed in Appendix I.

[d] STADD = Short-Term Absorbed Daily Dosage (STADD) = [(short-term exposure) × (absorption) × (acres treated/day) × (application rate)]/(70 kg body weight).

[e] SADD = Seasonal Average Daily Dosage (SADD) = [(long-term exposure) × (absorption) × (acres treated/day) × (application rate)]/(70 kg body weight).

Assumptions: maximum rate on product label, 0.5 lb/acre; dermal absorption is 26.3% (Ngo, 2015) ; inhalation absorption is 100% (Frank, 2008); body weight is 70 kg (Thongsinthusak *et al.*, 1993); daily acres treated are 1,200 acres for M/L and aircraft application for cotton (U.S. EPA, 2001); daily acres treated for flagging for aerial applications are 350 acres (U.S. EPA, 2001).

Table 5. Exposure Rates and Short-Term and Seasonal Exposure Estimates for Workers Handling Dicrotophos in Support of Ground boom Applications

Handler Task	Short-Term (µg/lb AI handled)		Long-Term (µg/lb AI handled)		STADD [c] (mg/kg/day)			SADD [d] (mg/kg/day)		
	Dermal	Inhalation	Dermal	Inhalation	Dermal	Inhalation	Total	Dermal	Inhalation	Total
M/L [a]	50.8	0.437	18.3	0.157	0.0191	6.25×10^{-4}	0.0197	6.86×10^{-3}	2.25×10^{-4}	7.09×10^{-3}
Applicator [b]	20.8	0.145	7.48	0.0522	7.82×10^{-3}	2.08×10^{-4}	8.03×10^{-3}	2.81×10^{-3}	7.46×10^{-5}	2.89×10^{-3}

[a] Abbreviations: M/L = mixer/loader. M/Ls using engineering controls (ECs) are required to wear long-sleeved shirt and long pants, chemical resistant footwear and socks. ECs include task-specific PPE, protective eyewear, and use of a closed-system for removing and transfer of pesticide from shipping container to mixing tanks and/or application equipment. M/Ls using ECs are also required to use chemical-resistant gloves and chemical-resistant apron. M/Ls are required to use a closed system for removing and transfer of pesticide from shipping container to mixing tanks and/or application equipment. M/Ls are required to wear chemical-resistant gloves. Estimates are based on scenario #6 from Beauvais *et al.* (2007) with additional protection factors of apron, chemical-resistant footwear, and eyewear, as detailed in Appendix I.

[b] Applicators using ECs are required to wear long-sleeved shirt and long pants, chemical resistant footwear and socks. Applicators using motorized ground equipment must use an enclosed cab that meets WPS for dermal protection. Applicators are also required to wear label-indicated type of respirator or use an enclosed cab that provides equivalent or greater respiratory protection as the specified respirator. Gloves are not specifically required for applicators within the enclosed cab. Estimates are based on scenario #12 from Beauvais *et al.* (2007) with additional protection factors of chemical-resistant footwear, as detailed in Appendix I.

[c] STADD = Short-Term Absorbed Daily Dosage (STADD) = [(short-term exposure) × (absorption) × (acres treated/day) x (application rate)]/(70 kg body weight).

[d] SADD = Seasonal Average Daily Dosage (SADD) = [(long-term exposure) × (absorption) × (acres treated/day) × (application rate)]/(70 kg body weight).

Assumptions include:
Maximum rate on product label, 0.5 lb/acre; dermal absorption is 26.3% (Ngo, 2015); inhalation absorption is 100% (Frank, 2008); body weight is 70 kg (Thongsinthusak *et al.*, 1993); daily acres treated are 200 acres for M/L and application via motorized ground equipment for cotton (U.S. EPA, 2001).

Occupational Post-application (Re-entry) Exposure

In determining post-application dermal exposures to dicrotophos, dislodgeable foliar residue (DFR) and transfer coefficients (TCs) were used. DFR is the foliar residues of pesticide that may be removed from both sides of treated leaf surfaces using aqueous surfactant and is considered available for field worker exposure. DFR is a measured value for a particular active ingredient (AI) formulation and crop. TC is a ratio of dermal exposure (mg/day) to exposure time and dislodgeable foliar residue (DFR) contacted by workers.

ExpoSAC Policy 3 provides recommended TCs for agricultural and commercial activities which may be used in post-application exposure assessments (U.S. EPA, 2013c). U.S. EPA-recommended TC for hand weeding (hand weeding, thinning and similar contact activities) of cotton crops, described as smooth-leaf field crop, is 70 cm^2/hr. Mechanical cotton harvesting occurs following defoliation, with potential exposure resulting from contact to cotton bolls. U.S ExpoSAC Policy 3 also provides non-foliar TCs for mechanical harvesting of cotton. Estimates of dislodgeable residue on cotton bolls (µg AI/gm cotton boll) are necessary to calculate this exposure. Non-foliar (cotton boll) residue data was not available, although exposure is expected to be minimal for this scenario. The U.S. EPA-recommended TC for cotton scouting is 210 cm^2/hr. However, the exposure assessment for cotton scouting uses a TC value of 2000 cm^2/hr (Frank, 2009a). This particular TC value was derived from a series of studies in which several OPs were applied to cotton and the potential dermal TCs were summed for the whole body of cotton scouts (Dong, 1990).

Cotton scouting is the representative scenario for addressing post-application exposures. Cotton scouts, including licensed crop advisors, enter cotton fields on foot, examining leaves and other plant parts for pests and evidence of pest damage. Exposure from cotton scouting is expected to be higher than that of other post-application scenarios such as hand weeding, as indicated by the TC. Thus, exposure and risk assessment for the scenario of cotton scouting should cover other post-application scenarios. With a label-required 30-day pre-harvest interval and DFR values reported to be below the limit of quantification (LOQ) by 14 days post-application, exposure from mechanical harvesting is expected to be negligible. We estimated potential exposure to cotton scouts of 5.05×10^{-3} mg/kg/day for short term exposures and 3.01×10^{-4} mg/kg/day for seasonal exposures, as presented in Table 6. These estimates are for the dermal route of exposure, as the inhalation route is assumed to be insignificant.

This exposure assessment utilized DFR data from the same study employed by U.S. EPA for estimating cotton scout exposure to dicrotophos (Prochaska, 1998) . This study reported a DFR of 0.5 lbs AI/acre applications to cotton at one site each in Mississippi and Texas. After the first application, average DFR values dropped from the highest value on Day 0 (i.e., immediately after the application) to below the LOQ on Day 14 at both sites. The highest average DFR values were 0.422 µg/cm^2 and 1.001 µg/cm^2 at the Mississippi and Texas sites, respectively.

Similarly, average DFR values dropped from the highest value on Day 0 after the second application at both sites. However, only the values of Texas site dropped below the LOQ at Day 14; the values of Mississippi site dropped below the LOQ at Day 7. The highest average DFR values measured following the second application were 0.180 $\mu g/cm^2$ and 0.343 $\mu g/cm^2$ (6.13% percent of the application rate) at the Mississippi and Texas sites, respectively. There were concerns regarding the appropriateness and reliability of data collected during the Mississippi study due to precipitation. Therefore, only DFR values measured from cotton crops in Texas were used for estimating worker exposure.

Following the approach of U.S. EPA (2014), DFR data from the first application in Texas were used for calculating residues on the leaves of treated cotton, and the resulting linear regression equation is shown as follows:

$$\mathbf{Ln\ (DFR) = -0.403t - 0.059}$$

The linear regression gave the following first order curve:

$$\mathbf{DFR_t = 0.936 \times e^{-0.403t}}$$

The DFR value on day 6 – the earliest day permitted for reentry into treated fields – is used to evaluate short-term dermal exposure potentials. For seasonal dermal exposure, scouting activities were expected to be performed at any time after application. Exposures were estimated for average reentry times of the reentry interval (REI) plus 7-10 days (Beauvais, 2008). In this case, the predicted DFR level was calculated for Day 13 (REI plus 7 days). This predicted level is assumed to be the average DFR level individuals who enter previously treated fields to perform scouting tasks would encounter during one cotton growing season. The default for daily work hours for cotton scouts is 8 hours/day.

Cotton industry guidance instructs scouts to inspect fields at least once a week (Bacheler, 2013; UGA, 2015) and prompts scouts to use appropriate PPE if entering treated fields prior to expiration of the REI (Foshee, 2012). Early entry to treated areas while a REI is in effect is allowed for certain activities, provided the label and Worker Protection Standard (WPS) for Agricultural Pesticides [40 CFR Part 170.603] conditions are met. Some of these permissible activities include: 1) entry with no contact; 2) short-term activities; 3) agricultural emergencies; 4) activities for limited contact; and, 5) irrigation activities. Additionally, no such entry is allowed during the first 4 hours following application. There are PPE requirements for early entry involving contact with plants, soil, water, or anything that has been treated. The PPE consists of coveralls worn over long-sleeve shirt and long pants, chemical-resistant gloves, chemical-resistant footwear plus socks, protective eyewear, and chemical-resistant headgear for

overhead exposure. Cotton scouts entering treated areas prior to expiration of the REI would be required to wear such PPE.

Potential short-term exposures to cotton scouts entering treated fields prior to the expiration of the REI while utilizing required PPE were estimated for the first day post-treatment, Day 1 (common practice for cotton scouts). The estimated value of 3.76×10^{-3} mg/kg/day was a lower than estimates of exposure for scouts entering treated fields without PPE 6 days post-application (5.05×10^{-3} mg/kg/day). As such, scouts wearing PPE during reentry into treated fields prior to the expiration of the REI are expected to have lower short-term and seasonal exposures than those entering after the REI. A 90% protection factor for PPE was applied to calculations for reentry prior to expiration of the REI.

The label also specifies that some certified crop advisors and persons performing crop advising tasks under their direct supervision, may be exempt from certain provisions of the WPS [40 CFR Part 170] if they meet the requirements for such exemption as listed in the WPS [40 CFR Part 170.104(b) and 170.204(b)]. With the exception of sweet corn, pest control/crop advisors reported scheduling inspections to avoid field entry during REIs (Spencer *et al.*, 2006). Crop advisors also reported informing scouts of fields that were under REI and trying to schedule inspections around REIs.

Table 6. Estimates of Dermal Exposure for Cotton Scouts Following Reentry into Dicrotophos-Treated Fields

Task	TC [a] (cm^2/hr)	DFR_6 [b] (µg/cm^2)	STADD [c] (mg/kg/day)	DFR_{13} [d] (µg/cm^2)	SADD [e] (mg/kg/day)
Scouting	2000	8.41×10^{-2}	5.05×10^{-3}	5.01×10^{-3}	3.01×10^{-4}

[a] TC = transfer coefficient. TC value for cotton scouting is taken from Frank (2009a).

[b] The linear regression equation of Ln (DFR) = -0.403t – 0.059 gave the first order curve of $DFR_t = 0.936 \times e^{-0.403t}$. DFR at day 6 was attributed to short-term exposures since this is the earliest time of reentry into a previously treated field (REI of 6 days).

[c] STADD = [Short-Term Absorbed Daily Dosage = (DFR_6) × (TC) × (work hours/day) × (dermal absorption)] ÷ [70 kg body weight]; DFR = dislodgeable foliar residue.

[d] DFR_{13} is the DFR at the average reentry interval, assumed to be the expiration of REI plus 7 days (Zhao and Formoli, 2005)

[e] Seasonal Average Daily Dosage (SADD) = [(DFR_{13}) × (TC) × (work hours/day) × (dermal absorption)] ÷ [70 kg body weight].

The daily work hours for cotton scouting are assumed to be 8 hours/day by default. The dermal absorption of 26.3% is used for this exposure assessment (Ngo, 2015). DFR data from registrant-submitted study was used for these estimates (Prochaska, 1998).

Residential Exposure of Adults and Children to Spray Drift

Label instructions for BIDRIN® 8 indicate aerial and ground applications. With these application methods, drift and deposition of dicrotophos to nearby residential sites or public areas such as schools, may occur. As a result, there is potential for exposure to adults and children (non-occupational bystanders) with indirect exposure (dermal contact, for example) with areas contaminated with drift deposition and/or with direct exposure (inhalation) to airborne materials, including aerosols. For evaluating bystander exposure to spray drift, this exposure assessment employed two computer models that were previously employed by HHA for estimating off-site movement of chlorpyrifos: AgDRIFT and AGDISP (Barry, 2015) and a modified Standard Operating Procedure for Residential Pesticide Exposure Assessment by U.S. EPA (U.S. EPA, 2013b).

For assessing indirect exposure to spray drift for adults and small children, the residential turf post-application SOP is considered by U.S. EPA as the standard method (U.S. EPA, 2013b). That is, activities of adults and children on the contaminated lawn may result in transfer of the drift deposit from different surfaces to their skin. Children 1-2 years old are considered the most relevant and sensitive population on account of their developmental susceptibilities and behavioral tendencies. Children in this age group frequently exhibit hand-to-mouth and object-to-mouth behavior, thereby transferring residues from their hands directly into their mouths. Accordingly, incidental ingestion, inhalation, and dermal exposure were appraised for this specific population. Only potential dermal and inhalation exposures were addressed for adults. Estimated exposures to adults and 1-2 year old children resulting from aerial and ground applications of dicrotophos for various distances from a treated field are provided in Tables 7, 8, and 9. Additional details for the spray drift modeling are provided in Appendix II.

Spray Drift Exposure Estimates from Aerial Applications

Drift deposition exposure (in µg/kg/day) and inhalation exposure estimates (1 hour time-weighted average air concentrations in µg/kg/day) associated with two different aerial applications rates and by either fixed-wing AT802A airplane or a rotor-wing Bell 205 helicopter are shown in Table 7 for adults and Table 8 for children. Increases in application rate resulted in a corresponding increase in the drift exposure estimates regardless of the exposure route at different distances downwind from the edge of the treated field.

Spray Drift Exposure Estimates from Ground Applications

Table 7 also shows the drift exposure estimates (in µg/kg/day) for adults for two application rates with high-boom and low-boom ground boom application methods. For ground boom, the drift deposition estimate was the 50th percentile deposition, rather than the 90th percentile used by U.S. EPA. The rationale for this selection is detailed in Barry (2015) for modeling chlorpyrifos drift

deposition. Table 9 shows the drift exposure estimates of dicrotophos for children 1-2 years old. For both of these application methods and population subgroups, the drift exposure estimates increase with application rates, as expected. The higher drift exposure estimates from high-boom relative to low-boom are consistent with the difference in release height above the target application.

Table 7. Estimated Doses via Dermal and Inhalation for Adults at Various Distances from a Dicrotophos-Treated Field Using Aerial- and Ground-Based [a] Equipment

Method	App. Rate (lb/acre)	Equipment	Dermal Exposure at Various Distance Downwind from the Treated Fields (µg/kg/day)						
			10 (feet)	**25 (feet)**	**50 (feet)**	**100 (feet)**	**250 (feet)**	**500 (feet)**	**1000 (feet)**
Aerial	0.25	AT802A	6.23	5.36	4.30	3.00	1.58	1.04	0.753
		Bell 205 Helicopter	8.60	5.44	3.27	1.98	1.41	1.02	0.623
	0.5	AT802A	12.8	11.0	8.93	6.27	3.35	2.12	1.43
		Bell 205 Helicopter	17.6	11.2	6.89	4.28	2.95	1.97	1.06
			25 (feet)	**50 (feet)**	**75 (feet)**	**100 (feet)**	**150 (feet)**	**200 (feet)**	**250 (feet)**
Ground [a]	0.25	High-Boom	1.57	0.975	0.716	0.567	0.395	0.299	0.237
		Low-Boom	0.550	0.358	0.273	0.223	0.164	0.130	0.107
	0.5	High-Boom	3.13	1.95	1.43	1.13	0.789	0.598	0.474
		Low-Boom	1.10	0.716	0.547	0.445	0.327	0.259	0.214
			Inhalation of 1-Hour Air Concentration at Various Distance Downwind from the Treated Fields (µg/kg/day)						
			10 (feet)	**25 (feet)**	**50 (feet)**	**100 (feet)**	**250 (feet)**	**500 (feet)**	**1000 (feet)**
Aerial	0.25	AT802A	2.92	2.78	2.56	2.28	1.84	1.50	1.10
		Bell 205 Helicopter	3.63	3.16	2.77	2.40	1.92	1.47	0.988
	0.5	AT802A	5.18	4.89	4.47	3.89	3.02	2.34	1.53
		Bell 205 Helicopter	6.44	5.52	4.74	4.00	3.03	2.17	1.36

[a] Drift deposition estimates were derived using a 50th percentile horizontal deposition (Barry, 2015).

Table 8. Estimated Doses for Children of 1-2 Years Old at Various Distances from a Dicrotophos-Treated Field Using Aerial Application Equipment

Aircraft	Exposure Route	Appl. Rate (lb/acre)	Dose at Various Distance Downwind from the Treated Fields (µg/kg/day)						
			10 (feet)	25 (feet)	50 (feet)	100 (feet)	250 (feet)	500 (feet)	1000 (feet)
AT802A	Dermal	0.25	9.13	7.85	6.31	4.40	2.32	1.52	1.10
		0.5	18.8	16.2	13.1	9.19	4.91	3.11	2.10
	Hand-to-Mouth	0.25	0.722	0.621	0.499	0.348	0.184	0.120	0.0873
		0.5	1.49	1.28	1.04	0.727	0.388	0.246	0.166
	Object-to-Mouth	0.25	0.0222	0.0191	0.0153	0.0107	5.60×10^{-3}	3.70×10^{-3}	2.70×10^{-3}
		0.5	0.0456	0.0393	0.0318	0.0223	0.0119	7.50×10^{-3}	5.10×10^{-3}
	Soil Ingestion	0.25	1.60×10^{-3}	1.40×10^{-3}	1.10×10^{-3}	8.00×10^{-4}	4.00×10^{-4}	3.00×10^{-4}	2.00×10^{-4}
		0.5	3.30×10^{-3}	2.80×10^{-3}	2.30×10^{-3}	1.60×10^{-3}	9.00×10^{-4}	5.00×10^{-4}	4.00×10^{-4}
			Inhalation of 1-Hour Air Concentration at Various Distance Downwind from the Treated Fields (µg/kg/day)						
	Inhalation	0.25	7.39	6.97	6.49	5.76	4.68	3.82	2.81
		0.5	13.1	12.2	11.3	9.81	7.65	5.97	3.92
			Dose at Various Distance Downwind from the Treated Fields (µg/kg/day)						
			10 (feet)	25 (feet)	50 (feet)	100 (feet)	250 (feet)	500 (feet)	1000 (feet)
Bell 205 Helicopter	Dermal	0.25	12.6	7.97	4.80	2.95	2.07	1.49	0.913
		0.5	25.8	16.5	10.1	6.28	4.33	2.88	1.55
	Hand-to-Mouth	0.25	0.997	0.631	0.380	0.230	0.164	0.118	0.0722
		0.5	2.04	1.30	0.800	0.497	0.343	0.228	0.123
	Object-to-Mouth	0.25	0.0306	0.0194	0.0116	7.10×10^{-3}	5.00×10^{-3}	3.60×10^{-3}	2.20×10^{-3}
		0.5	0.0626	0.0400	0.0245	0.0153	0.0105	7.00×10^{-3}	3.80×10^{-3}
	Soil Ingestion	0.25	2.20×10^{-3}	1.40×10^{-3}	8.00×10^{-4}	5.00×10^{-4}	4.00×10^{-4}	3.00×10^{-4}	2.00×10^{-4}
		0.5	4.50×10^{-3}	2.90×10^{-3}	1.80×10^{-3}	1.10×10^{-3}	8.00×10^{-4}	5.00×10^{-4}	3.00×10^{-4}
			Inhalation of 1-Hour Air Concentration at Various Distance Downwind from the Treated Fields (µg/kg/day)						
	Inhalation	0.25	9.56	8.23	7.17	6.18	4.95	3.78	2.54
		0.5	17.0	14.4	12.3	10.3	7.81	5.59	3.49

Table 9. Estimated Doses for Children of 1-2 Years Old at Various Distances from a Dicrotophos-Treated Field Using Groundboom [a] Equipment

Method	Exposure Route	Appl. Rate (lb/acre)	Dose at Various Distance Downwind from the Treated Fields (µg/kg/day)						
			25 (feet)	50 (feet)	75 (feet)	100 (feet)	150 (feet)	200 (feet)	250 (feet)
High-boom	Dermal	0.25	2.01	1.23	0.892	0.698	0.475	0.351	0.269
		0.5	4.02	2.46	1.78	1.40	0.950	0.702	0.537
	Hand-to-Mouth	0.25	0.159	0.0974	0.0706	0.0552	0.0376	0.0278	0.0212
		0.5	0.318	0.195	0.141	0.110	0.0752	0.0556	0.0425
	Object-to-Mouth	0.25	4.88×10^{-3}	2.99×10^{-3}	2.17×10^{-3}	1.70×10^{-3}	1.15×10^{-3}	8.5×10^{-4}	6.5×10^{-4}
		0.5	9.75×10^{-3}	5.98×10^{-3}	4.33×10^{-3}	3.39×10^{-3}	2.31×10^{-3}	1.71×10^{-3}	1.30×10^{-3}
	Soil Ingestion	0.25	3.50×10^{-4}	2.10×10^{-4}	1.50×10^{-4}	1.20×10^{-4}	8.00×10^{-5}	6.00×10^{-5}	5.00×10^{-5}
		0.5	7.00×10^{-4}	4.30×10^{-4}	3.10×10^{-4}	2.40×10^{-4}	1.60×10^{-4}	1.20×10^{-4}	9.00×10^{-5}
			Dose at Various Distance Downwind from the Treated Fields (µg/kg/day)						
			25 (feet)	50 (feet)	75 (feet)	100 (feet)	150 (feet)	200 (feet)	250 (feet)
Low-Boom	Dermal	0.25	0.368	0.244	0.186	0.153	0.116	0.0909	0.0744
		0.5	0.735	0.488	0.372	0.306	0.231	0.182	0.149
	Hand-to-Mouth	0.25	0.0291	0.0193	0.0147	0.0121	9.15×10^{-3}	7.19×10^{-3}	5.88×10^{-3}
		0.5	0.0582	0.0386	0.0294	0.0242	0.0183	0.0144	0.0118
	Object-to-Mouth	0.25	8.90×10^{-4}	5.90×10^{-4}	4.50×10^{-4}	3.70×10^{-4}	2.80×10^{-4}	2.20×10^{-4}	1.80×10^{-4}
		0.5	1.79×10^{-3}	1.18×10^{-3}	9.00×10^{-4}	7.40×10^{-4}	5.60×10^{-4}	4.40×10^{-4}	3.60×10^{-4}
	Soil Ingestion	0.25	6.00×10^{-5}	4.00×10^{-5}	3.00×10^{-5}	3.00×10^{-5}	2.00×10^{-5}	2.00×10^{-5}	1.00×10^{-5}
		0.5	1.30×10^{-4}	8.00×10^{-5}	6.00×10^{-5}	5.00×10^{-5}	4.00×10^{-5}	3.00×10^{-5}	3.00×10^{-5}

[a] Drift deposition estimates were derived using a 50th percentile horizontal deposition (Barry, 2015).

EXPOSURE APPRAISAL

This exposure assessment was generated for the purpose of the FIFRA section 24(c) SLN label registration. Key distinctions exist for the estimates of exposure assessed between U.S. EPA and HHA for the use of dicrotophos on cotton plants. Different exposure assessment approaches account for many of the differences listed herein. For example, this assessment uses defaults and assumptions which may differ from those of U.S. EPA. The default adult body weight currently used by HHA is 70 kg (Thongsinthusak *et al.*, 1993), rather than 80 kg typically used by U.S. EPA (U.S. EPA, 2011). However, due to concerns about the neurodevelopmental effects of OPs in fetuses and children, and the uncertainty in the human dose-response relationship for neurodevelopmental effects, U.S. EPA is using the female adult body weight of 69 kg to estimate exposure to dicrotophos (U.S. EPA, 2015b). In addition, when estimating handler exposure, HHA uses the 90% UCL of the 95th percentile from the PHED database (Versar, 1995) rather than the U.S. EPA approach of using the mean values to assess exposures. Other differences in approaches to exposure assessment between HHA and U.S. EPA are listed in Tables 10 and 11.

Table 10. Comparison of Reentry Exposure Values Used by HHA and U.S. EPA

Parameters	Exposure Route	DPR	U.S. EPA
Body weight (kg)	N/A	70	69
Exposure duration (hr)	N/A	8	8
DFR_6 (µg/cm^2) [a]	dermal	8.41×10^{-2}	8.4×10^{-2}
Transfer coefficient (cm^2/hr)	dermal	2000 [b]	210 [c]
Absorbed dose (mg/kg/day) [d]	dermal	5.05×10^{-3}	2.05×10^{-3}
	inhalation	insignificant	N/A

[a] DFR on day 6 following application was calculated based on registrant-submitted study (Prochaska, 1998).
[b] Cited from Frank (2009a).
[c] U.S. EPA (2013c).
[d] This exposure value was not directly reported in the U.S. EPA report but was calculated from the following equation: dermal exposure = [DFR × TC × duration] ÷ [body weight]; N/A: Inhalation exposure for scouting was not reported in the U.S. EPA risk assessment (U.S. EPA, 2015b).

Table 11. Comparison of Handler Exposure Values Used by HHA and U.S. EPA

Application method	Worker	Parameters	Exposure route	Exposure term [a]	DPR [b]	U.S. EPA [c]
Aerial	M/L	Body weight (kg)			70	80
		Unit exposure (µg/lb AI)	dermal	Short term	50.8	8.6
				Long-term	18.3	
			inhalation	Short term	0.437	0.083
				Long-term	0.157	
		Acres treated (acre)			1200	1200
		Maximum rate (lb/acre)			0.5	0.5
		Exposure (mg/kg/day)	dermal	Short term	**0.115**	**0.0748**
			inhalation	Short term	**3.75×10^{-3}**	**7.22×10^{-4}**
	Applicator	Body weight (kg)			70	80
		Unit exposure (µg/lb AI)	dermal	Short term	39.9	2.08
				Long-term	14.3	
			inhalation	Short term	0.0916	0.0049
				Long-term	0.0329	
		Acres treated (acre)			1200	1200
		Maximum rate (lb/acre)			0.5	0.5
		Exposure (mg/kg/day)	dermal	Short term	**0.0899**	**0.0181**
			inhalation	Short term	**7.85×10^{-4}**	**4.26×10^{-5}**
	Flagger	Body weight (kg)			70	80
		Unit exposure (µg/lb AI)	dermal	Short term	326.2	11
				Long-term	117.3	
			inhalation	Short term	0.68	0.35
				Long-term	0.245	
		Acres treated (acre)			350	350
		Maximum rate (lb/acre)			0.5	0.5
		Exposure (mg/kg/day)	dermal	Short term	**0.215**	**0.027**
			inhalation	Short term	**1.70×10^{-3}**	**8.88×10^{-5}**
Ground boom	M/L	Body weight (kg)			70	80
		Unit exposure (µg/lb AI)	dermal	Short term	50.8	8.6
				Long-term	18.3	
			inhalation	Short term	0.437	0.083
				Long-term	0.157	
		Acres treated (acre)			200	200
		Maximum rate (lb/acre)			0.5	0.5
		Exposure (mg/kg/day)	dermal	Short term	**0.0191**	**0.0125**
			inhalation	Short term	**6.25×10^{-4}**	**1.2×10^{-4}**
	Applicator	Body weight (kg)			70	80
		Unit exposure (µg/lb AI)	dermal	Short term	20.8	5.1
				Long-term	7.48	
			inhalation	Short term	0.145	0.043
				Long-term	0.0522	
		Acres treated (acre)			200	200
		Maximum rate (lb/acre)			0.5	0.5
		Exposure (mg/kg/day)	dermal	Short term	**7.82×10^{-3}**	**7.39×10^{-3}**
			inhalation	Short term	**2.08×10^{-4}**	**6.23×10^{-5}**

[a] Both "short-term" and "seasonal" exposure rates were estimated for this exposure assessment. U.S. EPA used steady state values and did not differentiate between short and longer-term exposures; [b] Unit exposure values for each scenario are from Beauvais *et al.* (2007); [c] Dermal and inhalation exposure cited from Table 6.1.1 of the U.S. EPA risk assessment for dicrotophos (U.S. EPA, 2015b).

Assumptions and Defaults

HHA policy is to use the arithmetic mean as the measure of central tendency in exposure assessments (Powell, 2003). Environmental concentrations tend to follow a lognormal distribution (Ott, 1995). As such, the geometric mean is the measure of central tendency for the lognormal distribution (Aitchison and Brown, 1957). However, as stated in Powell (2003), the DPR policy is "Regardless of the shape of the underlying distribution, HHA uses the arithmetic mean, rather than the geometric mean or median. Although it can be argued that the latter statistics better indicate the location of the center of a skewed distribution, it is not the location that is of interest in exposure assessment but the expected magnitude of exposure."

HHA uses the maximum application rate in potential exposure calculations. In the case of BIDRIN 8®, that value is 0.5 lbs/acre. Default values for acreage treated or amount of pesticide handled under various scenarios are based on ExpoSAC Policy 9.1 (U.S. EPA, 2001). Another point of divergence includes the approach to dermal absorption. HHA does not currently have a formal policy of *in vitro* dermal absorption data for use in risk assessment. For the purpose of this SLN product label review for BIDRIN® 8, the registrant-submitted dermal absorption studies for dicrotophos were evaluated under the "triple-pack" criteria as explained earlier in this document and in Appendix III.

In the absence of adequate chemical-specific data addressing the inhalation and absorption of airborne pesticides, HHA assumes 100% as the default inhalation retention/absorption value (Frank, 2008). The default adult body weight of 70 kg and default 1-2 year child body weight of 13 kg are utilized for this exposure assessment (Thongsinthusak *et al.*, 1993), rather than 80 kg for adults and 11.4 kg for children 1-2 years by U.S. EPA (U.S. EPA, 2011).

Use of PHED data

HHA differs from U.S. EPA in its approach to the use of PHED data. HHA considers PHED to have limitations as a generic database. It combines measurements from diverse studies involving different protocols, analytical methods and residue detection limits. Most dermal exposure studies in PHED use the patch dosimetry method of Durham and Wolfe (1962). This is, residues (in $\mu g/cm^2$) on small patches placed on different parts of the body and are multiplied by the surface area of the body part to extrapolate its exposure (in µg). These body part estimates are then summed to provide a total body exposure estimate. Some studies measured exposure only to selected body parts such as the hands, arms and face. As a consequence, the dermal exposure estimates for different body parts may be based on data from different studies. In addition, exposure scenarios are not completely characterized in the PHED database, confounding assessment of the match between a given subset and the exposure scenario it is intended to represent. Finally, assumptions underlying the use of generic data may be inappropriate in some cases, including, 1) exposure is primarily a function of the pesticide application

method/equipment and formulation type, and not of the physical/chemical properties of the specific AI; and, 2) exposure is proportional to the amount of AI handled.

HHA uses the 90% upper confidence limit (UCL) on an exposure statistic in order to account for some of the uncertainty inherent in using PHED and to increase our confidence that exposures are not underestimated. Estimating a confidence limit requires knowing the mean and standard deviation. PHED reports the mean of total dermal exposure, but only the coefficients of variation for separate body regions. Because the sample sizes per body region differ and because the correlations among body regions are unknown, the standard deviation of total dermal exposure cannot be calculated. In order to approximate the confidence limit for the 95th percentile, HHA makes the assumption that the population of total exposure is lognormally distributed across persons and has a population coefficient of variation of 100 percent. The method of approximation described in Powell (2007) uses the fact that the confidence limit for the 95th percentile (or for the mean) is a constant multiple of the arithmetic mean in any lognormal distribution with a given coefficient of variation. As such, any of these underlying assumptions could be false and result in incorrect UCLs.

HHA uses the 9o% UCL on the arithmetic mean when using PHED to estimate seasonal or annual exposure. As with short-term exposure estimates based on PHED subsets, a multiplier corresponding to the median sample size over body regions is used. If the median sample size is greater than 15, the multiplier is 1 (Powell, 2002).

Handler Exposure Database Estimates

HHA bases exposure estimates for workers handling dicrotophos on PHED. For some scenarios, including mixer/loader using closed systems, flaggers, and ground boom applicators with enclosed cabs, U.S. EPA also relies on data from PHED. However, for aerial applicators, U.S. EPA exposure estimates are based on newer data supplied by the Agricultural Handlers Exposure Task Force (AHETF). Recently, U.S. EPA released a table summarizing data used to estimate handler exposures (http://www.epa.gov/pesticide-science-and-assessing-pesticide-risks/occupational-pesticide-handler-exposure-data) (U.S. EPA, 2015c). For many handler scenarios, U.S. EPA no longer relies on PHED and instead uses newer data. DPR is reviewing newer studies included in U.S. EPA's Occupational Pesticide Handler Unit Exposure Surrogate Reference Table. Data from those studies will be used by DPR as appropriate when this review has been completed. The additional uncertainties from relying on older PHED data for aerial applicator exposure estimates will be considered during the mitigation phase.

Post-application Exposure Estimates

For post-application exposures, HHA considers the TCs presented by U.S. EPA Policy 3 (U.S. EPA, 2013c) appropriate for use in the dicrotophos exposure assessment, with the exception of

cotton scouting. Where the U.S. EPA recommends a TC of 210 cm^2/hr for cotton scouting (categorized under smooth-leaf field crops, scouting in row conditions), this exposure assessment uses the TC value of 2000 cm^2/hr (Frank, 2009a). This particular TC value was derived from a series of studies in which several OPs were applied to cotton and the potential dermal TCs for the whole body were summed for cotton scouts (Dong, 1990).

Spray Drift Exposure

Similar to U.S. EPA, this exposure assessment employed state-of-the-art computer model (AgDRIFT and AGDISP) coupled with the latest version of the U.S. EPA Residential Exposure Assessment Standard Operating Procedures for characterizing the non-occupational bystanders' exposure to spray drift of dicrotophos. Accordingly, the intrinsic uncertainties associated with these modeling and exposure computational methodologies (e.g., assumptions) will be translated into bystanders' exposure estimates of dicrotophos based on the manner in which these computer models and SOP were applied. Intrinsic uncertainties associated with these computer models and the SOP are detailed in the original memorandum (Barry, 2015). Therefore, the focus of the following discussion is to evaluate the uncertainties of exposure estimates based on specific choices made in using these models and formulas to estimate exposure.

For modeling spray drift, the input parameters were tailored to match the actual field operation and meteorological conditions that are expected to give the highest drift deposition and air concentration estimates in California (Barry, 2015). Hence, these exposure estimates of dicrotophos can be considered as the realistic upper bound values anticipated in California. Unlike the aerial application, the available computer models are unable to generate the air concentration of dicrotophos from ground boom. However, studies showed that the ambient air concentrations of other organophosphates like chlorpyrifos, measured after a ground based application could be similar (within a factor of ~2) to the simulated values from an aerial application (CARB, 1998). This observation suggests that ground based application methods may be as important as those of aerial application in contributing to the airborne dicrotophos at locations away from the treated field. The lack of air concentration estimates for ground boom application leads to an underestimate of exposure and risk for bystanders to these applications.

This assessment employed the same computer modeling and post-application exposure assessment approaches as U.S. EPA. For the aerial application, U.S. EPA used AgDRIFT while HHA used AGDISP. The AgDRIFT ground boom model is an empirical model and therefore incapable of generating values for air concentration. The lack of air concentration estimates for ground boom applications results in an underestimate of exposure and risk for bystanders close to the edge of a ground boom-treated field. Other details of model choices are discussed in Barry (2015) for the estimation of chlorpyrifos deposition and air concentrations.

In addition to the difference in model choice, different model parameters were employed in this exposure assessment due to certain agricultural practices and situations in California (Barry,

2015). These include the type of commonly used aircraft for aerial spray (e.g., AT 802A fixed wing aircraft), number of swathes to cover the application size (e.g., 50 swathes), and meteorological conditions (20% relative humidity and 90° F). For these reasons, a direct comparison of drift exposure estimates from this exposure assessment and U.S. EPA's (2015b) may not be straightforward.

"Take-home" Dust Exposures

Although pesticide residues in household dust appear to be a source of residential exposure, particularly for children, urinary metabolites of OP pesticides were not shown to be clearly associated with household dust levels (Lu *et al.*, 2000; Fenske *et al.*, 2002; Weppner *et al.*, 2006). Homes in proximity to pesticide-treated farmlands are found to have higher OP pesticide residues in house dust, suggesting pesticide drift to be a contributor to residential exposures (Simcox *et al.*, 1995; Lu *et al.*, 2000; Fenske *et al.*, 2002). To a lesser degree, pesticide levels of house dust were also associated with the "take home" scenario where pesticide residue are transferred from the workplace via work clothing, shoes, vehicles, and tools.

Mixers/Loaders and applicators are required to use closed systems to minimize exposure to dicrotophos. In addition, the label instructs user to remove and replace contaminated clothing and keep/wash the PPE separate from other laundry. Clothing that has been drenched or heavily contaminated is to be discarded and not reused. Such procedures may help to minimize "take home" residues of dicrotophos into the residential household setting. The tracking of dicrotophos residues into residential homes on contaminated footwear may be a source of dicrotophos exposure. However, this exposure is anticipated to be lower than exposures related to residential drift deposition.

CONCLUSIONS

Currently, there are no dicrotophos-containing products registered for use in the State of California. This exposure assessment was completed by the Human Health Assessment Branch (HHA) of the California Department of Pesticide Regulation (DPR) to address potential human exposures resulting from use of BIDRIN® 8, a water miscible formulation consisting of 82% dicrotophos, as part the review process for a FIFRA section 24(c) Special Local Need (SLN) label registration. The proposed 24(c) SLN product label indicates late season use, from first bloom to 30 days prior to harvest, for the control of the brown stink bug in Imperial, Riverside, and San Bernardino Counties.

Dicrotophos is an organophosphate (OP) pesticide with broad spectrum insecticidal activity and is a federal registered "restricted use" pesticide intended for closed-system delivery to cotton fields via aerial and ground equipment. Based on the 24c SLN label-specified uses of

dicrotophos, this exposure assessment evaluated only the acute and seasonal exposures in humans. Longer term exposures (i.e., annual/lifetime) were not anticipated. Exposure to dicrotophos may occur through dermal contact and inhalation in the occupational setting. Exposure may also occur in the residential setting from spray drift and take-home dust. The general population may also be exposed by ingestion of food with dicrotophos residue (TOXNET, 2016).

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APPENDIX I

PHED Data Subsets and Calculated Exposure Rates for Handler

Subsets of the data were selected from PHED for specific or similar application methods and formulation types to represent actual scenarios and active ingredients being evaluated. HHA uses estimates from PHED data subsets, selected for each scenario based upon certain criteria such as data quality, test material, and task specification, and adjusted in accordance with HHA policy (Beauvais *et al.*, 2007). These adjustments include upper confidence limits for the mean and the 95th percentile calculated for each handler scenario data subset. This exposure assessment also accounts for various protection factors conferred by PPE and engineering controls that were not originally covered in these adjustments. These protection factor adjustments are provided in the table footnotes. Summary of results from PHED data subsets for each scenario used in this exposure assessment for dicrotophos are presented below in Tables 1a – 4b. Calculations for the exposure rates are also provided for each scenario.

Table 1a. Summary of Results from PHED Dermal Exposures for Scenario 6 Aerial and Groundboom Spray: Mixer/Loader, Closed System, Liquids

Patch Location	Mean Dermal Exposure (µg/lb AI) [a]	Coefficient of Variance	Geometric Mean	Number of Observations	Adjusted Dermal Exposure (µg/lb AI) [a]
Head (All) [b]	1.6959	121.3279	0.9508	22	0.423975 [c]
Neck. Front	1.5225	278.5222	0.2418	22	1.5225
Neck. Back	0.456	280.8991	0.0729	22	0.456
Upper Arms	1.3441	96.6967	0.7988	21	1.3441
Chest	1.8416	93.4405	1.0577	16	0.09208 [d]
Back	1.8416	93.4405	1.0577	16	1.8416
Forearms	0.5474	98.5203	0.3206	21	0.5474
Thighs	2.3398	81.9301	1.5773	16	1.228395 [e]
Lower Legs	1.292	85.7276	0.8778	21	1.292
Feet [f]	0.67184	NA	NA	NA	0.067184 [g]

[a] Mean dermal exposure for certain body regions (assuming long pants, long-sleeved shirt) were adjusted with protection factors for PPE if indicated.
[b] Subset criteria included actual and estimated head patches. All 22 head observations were actual.
[c] Adjusted with protection factor of 0.75 for use of protective eyewear (goggles).
[d] Adjusted with protection factor of 0.95 for use of chemical-resistant apron.
[e] Adjusted with protection factor of 0.95 for use of chemical-resistant apron.
[f] Estimated value based on mean subset for lower leg exposure rate (0.52 x 1.292).
[g] Adjusted with protection factor of 0.90 for use of chemical-resistant footwear.

Table 1b. PHED Data Subsets for Dermal and Inhalation Exposures and Calculated Exposure Rates for Scenario 6 Aerial and Groundboom Spray: Mixer/Loader, Closed System, Liquids [a]

Exposure Category	Mean Subset Exposure Rate (µg/lb AI handled)	Number of Observations in Subset	Short-term Exposure Rate (µg/lb AI handled) [b]	Long-term Exposure Rate (µg/lb AI handled) [c]
Dermal – Non-hand [d]	13.6	18 [e]	48.6	17.5
Dermal – Hand (with gloves) [f]	5.72	31	19.3	6.93
Inhalation	0.128	27	0.437	0.157
Total Exposure	19.5	--	68.3	24.6

[a] Results from subsets of Mixer/Loader data in the PHED and upper confidence limits (UCL) for mean and 95th percentile calculated from these results. All values rounded to three significant figures.
[b] UCL for 95th percentile exposure = 1/SQRT(2)*MEAN*EXP[Z(0.95)*0.8326 + Z(0.90)*0.8326/SQRT(n)]; Equation 5 in Powell (2007).
[c] UCL for arithmetic mean exposure = MEAN*EXP[Z(0.90)*0.8326/SQRT(n)]; Eq. 6 in Powell (2007).
[d] Dermal total includes addition of default feet value of 0.52 x (value for lower legs); ratio of feet/lower leg surface area (U.S. EPA, 1997).
[e] Effective sample size for number of dermal observations was estimated as the harmonic mean, weighted by the squared mean dermal exposure.
[f] Gloves assumed to provide 90% protection; exposure of gloved hands is calculated as one tenth exposure of bare hands.

Table 2a. Summary of Results from PHED Dermal Exposures for Scenario 7: Flagger, Liquid

Patch Location	Mean Dermal Exposure (µg/lb AI) [a]	Coefficient of Variance	Geometric Mean	Number of Observations
Head (All) [b]	11.3	127.5702	5.6188	18
Neck. Front	0.9533	134.3334	0.5146	18
Neck. Back	1.4111	215.8529	0.4931	18
Upper Arms	3.9285	195.1025	0.8284	28
Chest	5.1065	188.8378	1.0384	26
Back	5.1065	188.8378	1.0384	26
Forearms	1.802	179.5283	0.3837	28
Thighs	4.0404	308.6996	0.9165	26
Lower Legs	2.448	305.6618	0.612	28
Feet	1.27296	NA	NA	NA

[a] Mean dermal exposure for certain body regions, assuming long pants, long-sleeved shirt were worn.
[b] Subset criteria included actual and estimated head patches. All 22 head observations were actual.

Table 2b. PHED Data Subsets for Dermal and Inhalation Exposures and Calculated Exposure Rates for Scenario 7: Flagger, Liquids [a]

Exposure Category	Mean Subset Exposure Rate (µg/lb AI handled)	Number of Observations in Subset	Short-term Exposure Rate (µg/lb AI handled) [b]	Long-term Exposure Rate (µg/lb AI handled) [c]
Dermal – Non-hand [d]	37.4	21 [e]	131	47.2
Dermal – Hand (no gloves)	59.7	30	200.2	72.5
Inhalation	0.200	28	0.680	0.245
Total Exposure	97.3	--	331.9	119.9

[a] Results from subsets of Mixer/Loader data in the PHED, and upper confidence limits (UCL) for mean and 95th percentile calculated from these results. All values rounded to three significant figures.
[b] UCL for 95th percentile exposure = 1/SQRT(2)*MEAN*EXP[Z(0.95)*0.8326 + Z(0.90)*0.8326/SQRT(n)]; Equation 5 in Powell (2007).
[c] UCL for arithmetic mean exposure = MEAN*EXP[Z(0.90)*0.8326/SQRT(n)]; Equation 6 in Powell (2007).
[d] Dermal total includes addition of default feet value of 0.52 x (value for lower legs); ratio of feet/lower leg surface area (U.S. EPA, 1997).
[e] Effective sample size for number of dermal observations was estimated as the harmonic mean, weighted by the squared mean dermal exposure.

Table 3a. Summary of Results from PHED Dermal Exposures for Scenario 12: Groundboom Applicator, Closed Cab

Patch Location	Mean Dermal Exposure (µg/lb AI) [a]	Coefficient of Variance	Geometric Mean	Number of Observations	Adjusted Dermal Exposure (µg/lb AI) [a]
Head (All) [b]	0.2031	70.0148	0.1729	16	0.2031
Neck. Front	0.0647	234.6213	0.028	16	0.0647
Neck. Back	0.0179	67.0391	0.0153	16	0.0179
Upper Arms	0.4365	73.0355	0.3707	16	0.4365
Chest	0.355	0	0.355	8	0.355
Back	0.355	0	0.355	8	0.355
Forearms	0.2647	118.2849	0.187	16	0.2647
Thighs	1.337	50.6507	1.176	8	0.701925
Lower Legs	1.071	93.9309	0.7651	16	1.071
Feet [c]	0.55692	NA	NA	NA	0.055692 [d]

[a] Mean dermal exposure for certain body regions (assuming long pants, long-sleeved shirt) were adjusted with protection factors for PPE if indicated.
[b] Subset criteria included actual and estimated head patches. All 22 head observations were actual.
[c] Estimated value based on mean subset for lower leg exposure rate (0.52 x 1.071).
[d] Adjusted with protection factor of 0.90 for use of chemical-resistant footwear.

Table 3b. PHED Data Subsets for Dermal and Inhalation Exposures and Calculated Exposure Rates for Scenario 12: Groundboom Applicator, Closed Cab [a]

Exposure Category	Mean Subset Exposure Rate (µg/lb AI handled)	Number of Observations in Subset	Short-term Exposure Rate (µg/lb AI handled) [b]	Long-term Exposure Rate (µg/lb AI handled) [c]
Dermal – Non-hand [d]	4.66	10 [e]	18.2	6.53
Dermal – Hand (no gloves)	1.87	12	7.08	2.54
Inhalation	0.040	16	0.145	0.0522
Total Exposure	6.68	--	25.4	9.12

[a] Results from subsets of Mixer/Loader data in the PHED, and upper confidence limits (UCL) for mean and 95th percentile calculated from these results. All values rounded to three significant figures.
[b] UCL for 95th percentile exposure = 1/SQRT(2)*MEAN*EXP[Z(0.95)*0.8326 + Z(0.90)*0.8326/SQRT(n)]; Equation 5 in Powell (2007).
[c] UCL for arithmetic mean exposure = MEAN*EXP[Z(0.90)*0.8326/SQRT(n)]; Equation 6 in Powell (2007).
[d] Dermal total includes addition of default feet value of 0.52 x (value for lower legs); ratio of feet/lower leg surface area (U.S. EPA, 1997).
[e] Effective sample size for number of dermal observations was estimated as the harmonic mean, weighted by the squared mean dermal exposure.

Table 4a. Summary of Results from PHED Dermal Exposures for Scenario 18: Aerial Applicator, Closed Cab

Patch Location	Mean Dermal Exposure (µg/lb AI) [a]	Coefficient of Variance	Geometric Mean	Number of Observations	Adjusted Dermal Exposure (µg/lb AI) [a]
Head (All) [b]	0.4689	190.9362	0.2178	28	0.4689
Neck. Front	0.0413	164.4068	0.0239	28	0.0413
Neck. Back	0.033	181.4068	0.0169	28	0.033
Upper Arms	0.3274	44.4411	0.3117	16	0.3274
Chest	0.355	0	0.355	14	0.355
Back	0.355	0	0.355	14	0.355
Forearms	0.1452	35.124	0.139	10	0.1452
Thighs	0.382	0	0.382	14	0.20055
Lower Legs	0.2975	54.6555	0.273	16	0.2975
Feet [c]	0.1547	NA	NA	NA	0.01547 [d]

[a] Mean dermal exposure for certain body regions (assuming long pants, long-sleeved shirt) were adjusted with protection factors for PPE if indicated.
[b] Subset criteria included actual and estimated head patches. All 22 head observations were actual.
[c] Estimated value based on mean subset for lower leg exposure rate (0.52 x 1.071).
[d] Adjusted with protection factor of 0.90 for use of chemical-resistant footwear.

Table 4b. PHED Data Subsets for Dermal and Inhalation Exposures and Calculated Exposure Rates for Scenario 18: Aerial Applicator, Liquids, Closed Cockpit [a]

Exposure Category	Mean Subset Exposure Rate (µg/lb AI handled)	Number of Observations in Subset	Short-term Exposure Rate (µg/lb AI handled) [b]	Long-term Exposure Rate (µg/lb AI handled) [c]
Dermal – Non-hand [d]	2.56	17 [e]	9.22	3.32
Dermal – Hand (no gloves)	9.57	36	31.8	11.4
Inhalation	0.025	15	0.0916	0.0329
Total Exposure	12.2	--	41.1	14.8

[a] Results from subsets of Mixer/Loader data in the PHED, and upper confidence limits (UCL) for mean and 95th percentile calculated from these results. All values rounded to three significant figures.
[b] UCL for 95th percentile exposure = 1/SQRT(2)*MEAN*EXP[Z(0.95)*0.8326 + Z(0.90)*0.8326/SQRT(n)]; Equation 5 in Powell (2007).
[c] UCL for arithmetic mean exposure = MEAN*EXP[Z(0.90)*0.8326/SQRT(n)]; Equation 6 in Powell (2007).
[d] Dermal total includes addition of default feet value of 0.52 x (value for lower legs); ratio of feet/lower leg surface area (U.S. EPA, 1997).
[e] Effective sample size for number of dermal observations was estimated as the harmonic mean, weighted by the squared mean dermal exposure.

APPENDIX II

Drift Exposure Assessment of Non-Occupational Bystanders

In addition to worker exposure, this exposure assessment addresses the potential for dicrotophos spray drift exposures to individuals (i.e., bystanders) who are in the vicinity of the application site. To this end, this exposure assessment adopted the method of U.S. EPA (U.S. EPA, 2013b) of using spray drift modeling coupled with the post-application assessment of dermal and inhalation exposures. For the spray drift modeling, the computer models employed were AgDRIFT (spray drift regression model version 2.0.05) for groundboom applications and AGDISP for aerial applications. For the post-application assessment, U.S. EPA standard operating procedures (SOP) for residential exposure assessment were followed.

General technical description of the AgDRIFT and AGDISP models are published elsewhere (Teske *et al.*, 2002; Teske and Curbishley, 2013). The specific modeling parameters employed in this work was detailed in Barry (2015) for estimation of chlorpyrifos deposition and air concentrations. Briefly, these spray drift models predict the off-site deposition of dicrotophos occurring relative to the nominal application rate (i.e., drift fraction) downwind of an application. The aerial and groundboom are allowable application methods for use on cotton (U.S. EPA, 2015a). **Table A-1** shows the application types and model parameter values for use in estimating the drift deposition. These scenarios and parameter values were chosen to maximize the horizontal drift deposition estimates from spray drift under different application types. In addition to the deposition estimates, for the aerial applications, one hour time-weighted average air concentrations (unit mg/m^3) of dicrotophos at vertical heights of 1.7 ft and 5 ft (i.e., breathing zone heights) were generated by AGDISP for use in estimating inhalation exposure of small children and adults, respectively. Similar to the deposition estimates, these time-weighted average air concentrations are the highest possible air concentrations based on the parameters listed in **Table A-1**.

Table A-1. Application Type Scenarios for Dicrotophos Deposition Estimates

Application Type	Sub-Type	Parameter Value	Nozzle Droplet	No. of Swaths (Coverage) [b]
Aerial	Fixed-Wing (AT802A)	10 mph wind; 20% RH; 90°F [a]	Medium	50 [c] (206.6)
	Rotor-Wing (Bell 205)	10 mph wind; 20% RH; 90°F [a]	Medium	50 [c] (190.4
Groundboom	Low Boom	20 inches above the canopy	VF-to-F	20 [d] (18.6)
	High Boom	50 inches above the canopy	VF-to-F	20 [d] (18.6)

Abbreviations: VF-to-F, very fine to fine; RH, relative humidity
[a] Meteorological conditions contributed to the highest horizontal drift deposition (i.e., worst case condition).
[b] Equivalent square acreage covered by the total number of swaths.
[c] Each swath for AT802A fixed wing aircraft is 60 feet and Bell 205 helicopter, 57.6 feet.
[d] Each swath for low- and high-boom is 45 feet.

Evaluation of dermal and inhalation exposures of non-occupational bystanders to spray drift was based on a modified U.S. EPA residential SOP which incorporated off-site movement of pesticide from the results of AgDRIFT and AGDISP models (U.S. EPA, 2013b). The non-occupational bystander exposure to spray drift is built on the assumption that dicrotophos application may occur near residential sites or areas (e.g., schools) which the general public routinely access. Accordingly, the bystander exposures could occur indirectly via contact (e.g., dermal exposure) with the areas contaminated with the drift deposit and (or) directly via inhalation of the airborne material (e.g., aerosol).

For assessing indirect exposure to spray drift for adults and small children, the residential turf post-application SOP is considered by the U.S. EPA as the standard method (U.S. EPA, 2013b). That is, activities of adults and children on the contaminated lawn may result in transfer of the drift deposit from different surfaces to their skin. In addition to the contact exposure via skin, exposure to the drift deposit may occur via mouthing such as hand-to-mouth, object-to-mouth, and incidental soil ingestion for small children.

For estimating the dermal exposure from contaminated lawn, the following equation is employed.

$$\text{Dermal Dose} = \frac{\text{TTR} \times \text{TC} \times \text{ED} \times \text{AF} \times \text{CF}}{\text{BW}}$$

where

TTR : turf transferable residue (μg/cm^2)
TC : transfer coefficient (cm^2/hr): 180000 for adults and 49000 for children
ED : exposure duration (hr/day): 1.5 for both adults and children

AF : absorption factor (dermal): 1 for computational purpose
CF : conversion factor of 0.001 mg/µg
BW : body weight (kg): 70 kg for adults; 13 kg for 1-2 years old (Andrews and Patterson, 2000)

According to the U.S. EPA 2012 residential SOP (U.S. EPA, 2012b), in the absence of chemical-specific data, TTR can be estimated based on the following equation.

$$TTR_t = AR \times F \times (1-F_D)^t \times CF2 \times CF3$$

where

TTR_t : turf transferable residue on day t (µg/cm^2) ($TTR_t = TTR_0$; i.e., Day 0)
AR : application rate (lbs AI/ft^2 or lb AI/acre) (AR = 0.25 or 0.5 lb-AI/acre)
F : fraction of AI as transferable residue following application (F = 0.01)
F_D : fraction of residue that dissipates daily (unitless) ($F_D = 0$)
t : post-application day on which exposure is being assessed (t = 0)
CF2 : weight unit conversion factor (4.54×10^8 µg/lb)
CF3 : area unit conversion factor (1.08×10^{-3} ft^2/ cm^2 or 2.47×10^{-8} acre/cm^2)

For estimating exposures to drift deposit due to mouthing activities of small children, such as hand-to-mouth, object-to-mouth, and incidental soil ingestion, computational methods as defined in the U.S. EPA residential SOP were strictly followed (U.S. EPA, 2012b). Therefore, these computational methods are not reproduced in this exposure assessment.

For evaluating the inhalation exposure, breathing zone exposure concentrations of dicrotophos in adults and small children are needed for the two application types: aerial and ground boom. However, the empirical nature of the module in the AgDRIFT for ground boom precludes the generation of the needed breathing zone air concentrations. Accordingly, inhalation exposure calculations were performed only for the aerial application of dicrotophos.

APPENDIX III

Memorandum: Dicrotophos Triple-Pack Dermal Absorption Data Package Review

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DATE: December 3, 2015
SUBJECT: STUDY REVIEWS: DICROTOPHOS TRIPLE-PACK DERMAL ABSORPTION, DATA PACKAGE ID# 260917

Summary
This memorandum reviews two dermal absorption studies submitted by AMVAC Chemical Corporation in support of the 24© SLN registration of BIDRIN® 8 for use on cotton plants. Based on these studies, a recommendation regarding the human dermal absorption factor for estimating exposures to persons who come in contact with dicrotophos under label uses is provided.

BIDRIN® 8 contains 82% dicrotophos, or 8 lbs per gallon, as the active ingredient in a water miscible concentrate formulation. Dicrotophos, an organophosphate pesticide with broad spectrum activity, is both a Federally- and California-restricted pesticide delivered by closed system aerial and ground equipment.

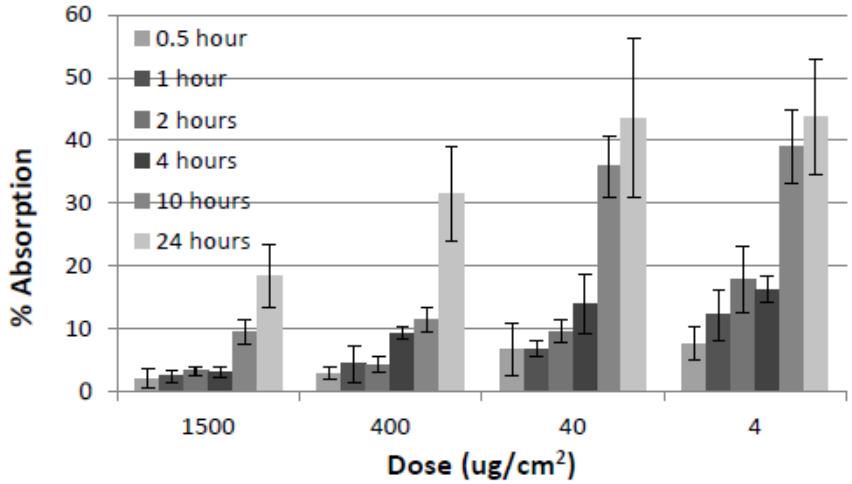
The two studies under review are "Dicrotophos: *In Vivo* Dermal Penetration Study in the Rat," hereafter referred to as "*In Vivo* Rat Study" (Gledhill, 1999), and "Dicrotophos: *In Vitro* Absorption Through Human and Rat Epidermis," hereafter referred to as "*In Vitro* Human and Rat Study" (Davies, 1999). These studies fulfilled the "triple-pack" requirements for determining human skin absorption of dicrotophos.

Overall, this assessment recommends an upper 95% confidence interval of the dermal absorption value, 26.3%, to be used in human health exposure and risk estimates for BIDRIN® 8. This value is derived from the above-mentioned studies with consideration being given to both absorbed and skin-bound residues (i.e., those bound to the *Stratum corneum* of the epidermis). Specifically, the "triple-pack" approach was employed for relating *in vitro* and *in vivo* animal data and applied the ratio to *in vitro* human data to derive a human *in vivo* dermal absorption value. The calculated 95% confidence interval approximates a human *in vivo* dermal absorption in the range of 11.8% to 26.3%.

Background

Percent absorption typically increases with decreasing dermal dose, as shown in **Figure 1,** which summarizes data from the *In Vivo* Rat Study (Gledhill, 1999). This decrease in dermal absorption at higher doses is thought to be the results of inundated absorption mechanisms. Although less clear, the *In Vitro* Human and Rat Study also showed a similar dose-response trend (Davies, 1999, data not shown).

Figure 1. *In Vivo* Rat Absorption of Dicrotophos



Based on an earlier evaluation of other studies finding absorption to be greater at lower doses, the lowest test dose recommended for use in experimental studies on dermal absorption is in the 1 to 6 µg/cm^2 range (Thongsinthusak, 1994). The lowest dose tested in the *In Vivo* Rat Study was 4 µg/cm^2. While the lowest nominal dose for the *In Vitro* Human and Rat Study was intended to be 4 µg/cm^2, the actual test dose was 9.66 µg/cm^2, making comparisons between the *in vivo* and *in vitro* studies less favorable. However, the percent absorption at 24 hours did not differ significantly between the two lowest doses *in vivo* (4 and 40 µg/cm^2), and between the two lowest doses *in vitro* for both rat and human tissues (9.66 and 43 µg/cm^2). For this reason, this

assessment will consider the *in vitro* data for use in estimating the *in vivo* human dermal absorption value.

This review finds the *In Vivo* Rat Study to be of high quality with acceptable and reliable data. Although the same conclusion cannot be expressed for the *In Vitro* Human and Rat Study, the data from this study may still be considered usable. It should be noted that, as opposed to the use of similar doses as employed in typical "triple pack" studies, these dermal absorption studies were conducted with two rather different doses: 4 $\mu g/cm^2$ (*in vivo*) and of 10 $\mu g/cm^2$ (*in vitro*). The data are summarized in the following table, **Table 1**, with details provided in the rest of this memorandum.

U.S. EPA utilized route-specific toxicity studies as the bases for their steady-state points of departure (2014) and therefore did not use absorption factors for exposure estimates. Nonetheless, U.S. EPA did adjust the dermal point of departure (2.1 mg/kg/day) using the ratio of the *in vitro* rat-to-*in vitro* human absorption (4.44) for an "adjusted dermal point of departure" of 9.33 mg/kg/day (2.1 mg/kg/day × 4.44).

As previously mentioned, HHA found the *In Vivo* Rat Study to be of high quality with reliable data. However, less confidence can be placed in the *In Vitro* Human and Rat Study due to absence of data points without providing explanation or justification and incomplete or inconsistent procedural and technical information. Since the *In Vitro* Human and Rat Study was completed in 1999, it also does not meet the requirement of demonstrating adequate solubility of the test compound in the receptor fluid (OECD, 2004). In addition, there appears to be a higher level of variability in the data values, with total recovery ranging from 79.9% to 132% throughout the study. For the lowest dose of 9.66 $\mu g/cm^2$, total recovery at 24 hours post-application ranged from 117% to 132% for the human tissue samples, with an average percent recovery of 124.7%. These high recovery values (i.e., > 110%) reduce the amount of confidence that can be placed on this study. One helpful aspect of the *In Vitro* Human and Rat Study is that the animal and human samples were conducted concurrently under the same experimental protocols. The use of the same test conditions is a fundamental principle in the "triple-pack" methodology, as *in vitro* test variables are recognized to greatly influence the test outcome.

Table 1. Dicrotophos Dermal Absorption Values Used by U.S. EPA and this Review.

	In Vitro Rat [a] (% Absorption)	*In Vitro* Human [a] (% Absorption)	*In Vivo* Rat [b] (% Absorption)	*In Vitro* [a] Rat to *In Vivo* [b] Rat	*In Vitro* [a] Rat to *In Vitro* [a] Human	"Equivalent" *In Vivo* Human (% Absorption)
U.S. EPA [c]	47.1	10.6	32.9	N/A	4.44	N/A
24 hours						
Reported "Absorbed" Dose [d]	37.2 ± 10.4	10.3 ± 3.0	32.9 ± 7.2	N/A	N/A	N/A
Residues in Epidermis or "skin"	16.7 ± 3.8	8.8 ± 0.6	2.9 ± 2.1	N/A	N/A	N/A
Residues in *Stratum Corneum*	N/A	N/A	7.9 ± 1.8	N/A	N/A	N/A
This Review [e]	53.9 ± 10.7	19.0 ± 2.8	43.7 ± 9.1	**0.88 – 1.6 [f]**	N/A	**11.8 – 26.3 [f]**
10 hours						
Reported "Absorbed" Dose [d]	53.1 ± 12.8	6.6 ± 7.5	28.0 ± 6.6	N/A	N/A	N/A
Residues in Epidermis or "skin"	17.6 ± 6.1	6.7 ± 1.9	3.3 ± 1.8	N/A	N/A	N/A
Residues in *Stratum Corneum*	N/A	N/A	7.8 ± 2.8	N/A	N/A	N/A
This Review [e]	70.6 ± 8.1	13.4 ± 9.1	39.0 ± 5.7	**1.5 – 2.1[g]**	N/A	**2.3 – 25.1[g]**

[a] Dermal dose was 9.66 µg/cm^2 (Davies, 1999); [b] Dermal dose was 4 µg/cm^2 (Gledhill, 1999); [c] Values used by U.S. EPA's risk assessment for dicrotophos (2014); *In vitro* values used by U.S. EPA appear to have been retrieved from a summary table of the study report, the values of which differed significantly from those derived using the raw data; [d] Absorbed values reported by the *In Vitro* Human and Rat Study (Davies, 1999) are concentrations detected in the receptor fluid, while values reported by the *In Vivo* Rat Study (Gledhill, 1999) are the sum of dicrotophos residues determined in the urine, feces, cage wash, carbon dioxide trap contents and charcoal trap extractions, GI tract contents, and carcass; [e] Values estimated from this review include residues detected in the *Stratum Corneum* and epidermis or application site skin, summed with the "absorbed" doses reported from respective study; [f] 95% confidence interval calculated using N=6, t-value =2.447; [g] same as "*f*", using N=5, t-value = 2.571; N/A = not applicable or not available.

Triple-Pack Dermal Absorption Method

The "triple-pack" approach correlates *in vitro* and *in vivo* animal, as well as *in vitro* human data to make inferences for an appropriate human dermal absorption factor value to be used in human health risk assessment. Various regulatory bodies take slightly different approaches to how to ratio or relate these *in vivo* and *in vitro* data. In this assessment, the ratio of *in vitro* animal data to *in vivo* animal data presents a means of determining the reliability of the *in vitro* test conditions to predict *in vivo* absorption.

$$\text{IF} \quad \frac{\text{Animal } \textit{in vitro}}{\text{Animal } \textit{in vivo}} \approx 1 \qquad \text{THEN} \quad \text{Human } \textit{in vitro} \approx \text{Human } \textit{in vivo}$$

This "triple-pack" approach suggests that the ratio of animal *in vitro* to *in vivo* dermal absorption is essentially one for the human *in vitro* data to be considered equivalent to *in vivo* human dermal absorption. The question then arises, as to how close to the value of one must this ratio be for the human *in vitro* data to be acceptable and representative of human *in vivo* absorption. This would require a limit or range to be defined for acceptable ratio values. At this time, we are proposing to use a 95% confidence interval (CI) to describe the uncertainty associated with relating *in vitro* to in *vivo* data (computational details are provided in the appendix).

Calculation of a 95% CI will be performed twice in the "triple-pack" approach. First, in defining the CI for the ratio of the mean values of *in vitro* to *in vivo* animal absorption, it can be determined, with 95% confidence, whether the ratio value statistically overlaps with the value of one. If this CI for the animal ratio satisfies the criterion of approximating the value of one, then the assumption is that the conditions of the *in vitro* assay are appropriate for estimating observed *in vivo* dermal penetration. Subsequent to satisfying this criterion, a second 95% CI is calculated for the mean *in vitro* human absorption. This calculation incorporates the relative errors from the animal data with the relative error from the *in vitro* human data to derive a range in which *in vivo* human dermal penetration is expected for dicrotophos. Data quality is accounted for to some degree, in that the sample size and data variance can affect the confidence interval size. For example, although the 95% CI of the *in vitro* to *in vivo* animal absorption ratio may overlap with the value of one, if the standard error of any of the datasets is large, the resultant upper-bound estimate for *in vivo* human absorption is increased.

Additionally, in this assessment, any residues determined in the *Stratum Corneum*, epidermis, and dermis are considered to be absorbed. By contrast, neither the study authors nor U.S. EPA used the skin-bound residues to calculate the dermal equivalent dose. By including the skin-

bound residues, the estimated dermal absorption is significantly increased from "absorbed" values reported in the study (**Table 1)**.

An exposure period of 24 hours was implemented in the *In Vitro* Human and Rat Study, with samples collected at 0.5, 1, 2, 4, 10, and 24 hours (these were exposure and sampling times for the *In Vivo* Rat Study). A sampling period of 24 hours is typically required to suitably characterize the absorption profile (OECD, 2004). For the 1:1000 dilution (4 or 9.66 $\mu g/cm^2$) test dose, the test dose with the most relevance to dermal exposure scenarios under the proposed uses, the absorption at 24 hours post-exposure was utilized for this assessment. Although it may be argued that 10 hours is a more relevant time-point for consideration of some scenarios, such as an 8 hour work day, it should be noted that the absorption values at 10 hours did not differ significantly from those at 24 hours at the two lowest doses (4 and 40 $\mu g/cm^2$ for the *In Vivo* Rat Study, and 9.66 and 43 $\mu g/cm^2$ the *In Vitro* Human and Rat Study). Furthermore, calculations for the 95% CI for the study data did not meet the "triple-pack" criteria of overlapping the value of one.

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Appendix to Memorandum

I. Application of the 95% Confidence Interval for Deriving Human Dermal Absorption

The 95% confidence interval (CI) calculations were developed by Kwok (2015) based on the principal of error propagation (Bevington and Robinson, 2003). The 95% CI was calculated for the ratio of the animal data and for the mean *in vitro* human dermal absorption. These mean values were determined from the data of submitted dermal absorption studies. The relative errors from the animal studies are incorporated with the relative error of the human *in vitro* data to calculate the total error and interval of values for the human *in vivo* dermal absorption estimate. An example of how this 95% CI is applied to *in vitro* human absorption values is provided at the end of this appendix.

A. Confidence Interval of *In Vitro*-to-*In Vivo* Animal Dermal Absorption Ratio (R)

$$\textit{In Vitro}:\textit{In Vivo}\ \text{Ratio (R)} = \frac{\textit{In Vitro}\ \text{Dermal Absorption (x)}}{\textit{In Vivo}\ \text{Dermal Absorption (y)}}$$

The error of R can be expressed approximately as

$$\Delta R = \frac{\partial R}{\partial x}\Delta x + \frac{\partial R}{\partial y}\Delta y$$

Partial derivatives of each variable are the function of the other variable

$$\frac{\partial R}{\partial x} = \frac{1}{y} \text{ and } \frac{\partial R}{\partial y} = \frac{-x}{y^2}$$

Therefore,

$$\Delta R = \frac{\partial x}{y} - \frac{x\partial y}{y^2}$$

$$\Delta R = \frac{\partial x}{x}\frac{x}{y} - \frac{\partial y}{y}\frac{x}{y}$$

$$\Delta R = \frac{\partial x}{x}R - \frac{\partial y}{y}R$$

$$\Delta R = R\left(\frac{\partial x}{x} - \frac{\partial y}{y}\right)$$

$$\left(\frac{\Delta R}{R}\right)^2 = \left(\frac{\partial x}{x} - \frac{\partial y}{y}\right)^2$$

$$\left(\frac{\Delta R}{R}\right)^2 = \left(\frac{\partial x}{x}\right)^2 + \left(\frac{\partial y}{y}\right)^2 - 2\left(\frac{\partial x}{x}\right)\left(\frac{\partial y}{y}\right)$$

can be expressed as

$$\frac{\sigma_R^2}{R^2} = \frac{\sigma_x^2}{x^2} + \frac{\sigma_y^2}{y^2} - 2\frac{\sigma_{xy}^2}{xy}$$

If the covariance is equal to zero, then

$$\left(\frac{\Delta R}{R}\right)^2 = \left(\frac{\partial x}{x}\right)^2 + \left(\frac{\partial y}{y}\right)^2$$

$$\sigma_R^2 = R^2\left(\frac{\sigma_x^2}{x^2} + \frac{\sigma_y^2}{y^2}\right)$$

$$\sigma_R = R\sqrt{\left(\frac{\sigma_x}{x}\right)^2 + \left(\frac{\sigma_y}{y}\right)^2}$$

Since $\frac{\sigma\sigma_{xx}}{x}$ and $\frac{\sigma\sigma_{yy}}{y}$ can be considered as relative uncertainties or errors (Err) of x and y, respectively, therefore the total error of R is given by:

$$\text{Err}(R) = \left(\frac{x}{}\right)\sqrt{(\text{Err}[x])^2 + (\text{Err}[y])^2\, y}$$

For *in vitro*-to-*in vivo* dermal absorption in rats, the 95% CI of R_{rat} is given by

$$R_{rat} \pm t^*\left(\frac{\sigma\sigma_{RR}}{\sqrt{NN}}\right)$$

where:
t* = the critical value of t at 95th confidence level
N = sample size

B. Confidence Interval of *In Vivo* Dermal Absorption in Humans

Assuming that *in vitro*-to-*in vivo* dermal absorption ratios in humans and animals are the same ($R_{rat} \approx 1 \approx R_{human}$), using the estimated Err (R_{rat}) and experimentally determined Err (x) (*in vitro* dermal absorption in humans), the estimated Err (y) (*in vivo* dermal absorption in humans) can be expressed as:

$$\text{Err (y)} = (yy) \sqrt{(\text{Err[x]})^2 + (\text{Err[R]})^2}$$

For *in vivo* dermal absorption in humans, the 95% CI of y is given by

$$y \pm t^* \frac{\sigma\sigma_{yy}}{\sqrt{NN}}$$

where:
t* = the critical value of t at 95% confidence level
N = sample size

II. Example for Application of the 95% Confidence Interval in Deriving Human Dermal Absorption

A. Confidence Interval of *In Vitro*-to-*In Vivo* Dermal Absorption Ratio (R)

Given: *In vitro* rat absorption (%): 53.9 ± 10.7 (data from triple pack studies)
***In vivo* rat absorption (%): 43.7 ± 9.1 (**data from triple pack studies)

$$\text{Err[x]} = 10.7/53.9 = 0.198$$
$$\text{Err[y]} = 9.1/43.7 = 0.208$$
$$R = x/y = 53.9/43.7 = 1.23$$

$$\text{Err (R)} = \frac{x}{} \sqrt{(\text{Err[x]})^2 + (\text{Err[y]})^2}\, y$$

Therefore, Err[R] = 0.35
The 95% CI of R: 0.88 – 1.59 (for N = 6 and t* = 2.447)

B. Confidence Interval of *In Vivo* Dermal Absorption in Humans

Given: *In vitro* human absorption (%): 19.0 ± 2.8 (data from triple pack studies)

$$\text{Err}[x] = 2.8/19.0 = 0.147$$
$$\text{Err}[R] = 0.35 \text{ (from above calculations)}$$

Assuming that R ≈ 1, the *in vivo* human absorption would be 19%

$$\text{Err}(y) = (yy) \cdot \sqrt{(\text{Err}[x])^2 + (\text{Err}[R])^2}$$

Therefore, Err [y] = 7.2
The 95% CI of y: 11.8 – 26.3% (for N = 6 and t* = 2.447)