(3)/OPP#34132 (4PPP)

A Note to Readers:

This report contains the recommendations for the 10-fold safety factor for each of the organophosphates. These recommendations were made by the Office of Pesticide Program's (OPP) FQPA Safety Factor Committee. This Committee is composed of staff from across Divisions in OPP and makes its recommendations to management for the final decision on the FQPA safety factor. The hazard assessment was provided by the HED Hazard Identification Assessment Review Committee (HIARC) and was considered along with the exposure data to determine if the available data are sufficiently reliable to permit reduction or removal of the 10-fold safety factor to protect infants and children from exposure to pesticides. The Committee also developed the recomendation for the application of the safety factor to the appropriate population subgroups (e.g., women of childbearing years, general population including infants and children) for each type of risk assessment (e.g., acute and chronic dietary, residential exposures) for each of the organophosates..

Scientific documents of this kind always reflect the work and analyses conducted at the time they are produced. It is common and appropriate that, as new information becomes available, additional analyses are performed, and/or Agency policy evolves, the conclusions may change.

We believe that the U.S. food supply is the safest in the world. Leading health experts recommend that people eat five servings of fruits and vegetables a day, along with a variety of foods. Through implementation of the Agency's tolerance reassessment program, as mandated by the Food Quality Protection Act, the food supply will become even safer.

August 06, 1998

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UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

06-AUG-1998

MEMORANDUM

SUBJECT: ***FQPA SAFETY FACTOR RECOMMENDATIONS FOR THE ORGANOPHOSPHATES*** (A Combined Report of the Hazard Identification Assessment Review Committee and the FQPA Safety Factor Committee)

FROM: Brenda Tarplee, Executive Secretary
FQPA Safety Factor Committee
Health Effects Division (7509C)
and
Jess Rowland, Executive Secretary
Hazard Identification Assessment Review Committee
Health Effects Division (7509C)

THROUGH: Ed Zager, Chairman
FQPA Safety Factor Committee
Health Effects Division (7509C)

TO: Margaret Stasikowski, Division Director
Health Effects Division (7509C)

Attached is a combined report of HED's Hazard Identification Assessment Review Committee (HIARC) and the FQPA Safety Factor Committee. This report includes the data presented in the July 7, 1998 Report of the HIARC, as well as the recommendations made by the FQPA Safety Factor Committee.

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FQPA SAFETY FACTOR RECOMMENDATIONS FOR THE ORGANOPHOSPHATES

A Combined Report of the
Hazard Identification Assessment Review Committee and the
FQPA Safety Factor Committee

HEALTH EFFECTS DIVISION
OFFICE OF PESTICIDE PROGRAMS
U.S. ENVIRONMENTAL PROTECTION AGENCY

August 6, 1998

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Committee Members in Attendance

Members present were: William Burnam, Richard Kiegwin, Ray Kent, Deborah McCall, Kathy Monk, Daniel Rieder, Jess Rowland, Brenda Tarplee (Executive Secretary), Edward Zager (Chairperson).

Hazard Identification Assessment Review Committee member present as observer: Susan Makris.

Report Preparation:

Brenda Tarplee, Executive Secretary
FQPA Safety Factor Committee

Jess Rowland, Executive Secretary
Hazard Identification Assessment Review Committee

I. INTRODUCTION

The Hazard Identification Assessment Review Committee (HIARC) convened on May 12 - 14, 1998 for a comprehensive review of 40 Organophosphates which were originally reviewed by this Committee from September 1997 through May 1998.

The FQPA Safety Factor Committee (FQPA SFC) met on June 15 and 16, 1998 to evaluate hazard and exposure data for the organophosphates and to determine whether the data on each organophosphate are sufficiently reliable to permit reduction or removal of the 10-fold safety factor mandated by the Food Quality Protection Act of 1996 to protect infants and children from exposure to pesticides.

This report includes the results of both Committee meetings, including the recommendations for the FQPA safety factor (by the FQPA SFC) and a listing of additional uncertainty factors (by the HIARC) for use in the risk assessment process for the organophosphates.

II. HAZARD ASSESSMENT

HIARC's objective for this reassessment was to evaluate the following factors for consistency: 1) assessment of neurotoxicity studies for evidence of neuropathology; 2) quantitative and qualitative assessment of developmental and reproductive toxicity studies for enhanced susceptibility of infants and children as required by FQPA; 3) use of literature data in hazard identification; 4) identification of data gaps; 5) criteria used in triggering a developmental neurotoxicity study; 6) recommendations on FQPA Safety Factor to the FQPA Safety Committee; 7) the toxicological endpoints and doses for acute and chronic dietary as well as occupational and residential exposure risk assessments; 8) selection of dermal absorption factors for dermal risk assessments; and 9) application of FIFRA-related uncertainty factors.

Determination of susceptibility was performed for each pesticide on a case-by-case basis employing a weight-of-evidence assessment. The two primary concerns or factors that contributed to the decision-making process were: 1) enhanced **susceptibility** of the developing organism or offspring as might be observed in prenatal developmental toxicity studies in rodents and non-rodents, as well as multi-generation reproduction studies in rodents. The entire toxicity data base; particularly the hen and rat neurotoxicity studies, was evaluated for evidence of neuropathology (e.g., decreases in brain weights), which might be indicative of increased susceptibility of the developing nervous system; and 2) **uncertainty** related to the absence of complete toxicity data for the assessment of potential effects on infants and children.

The HIARC did not consider these two factors to be separate entities, but rather aspects of an information continuum that defined the uncertainties in how pesticides might affect humans. Thus in recommending an FQPA Safety Factor, an evaluation of susceptibility and uncertainty

issues might be altered by weight-of-evidence considerations such as: the severity of toxic effects in offspring in comparison to severity of maternal effects; a characterization of the dose-response curve for effects related to offspring; concordance of treatment-related effects between species and/or strains; knowledge of mode of action; and the level of confidence in the data base or critical studies.

The toxicology data base was evaluated for the neurotoxic, developmental and reproductive toxic potential of the 40 organophosphates. Of the 40, the data base was inadequate for Chlorpyrifos-methyl, Dicrotophos, and Temephos and no data were available for Fonofos, Isazophos, and Sulfotepp.

1. **Evaluation of Neurotoxicity**

The neurotoxicity data requirements include an acute delayed neurotoxicity study in hens, an acute neurotoxicity study in rats, and a subchronic neurotoxicity study in rats.

The acute delayed neurotoxicity study in hens was evaluated for organophosphate-induced delayed neurotoxicity (OPIDN); assessment of inhibition of acetylcholinesterase; and neurotoxic esterase (NTE); and histopathological assessment of brain, peripheral nerve, and spinal cord. Acute and the subchronic neurotoxicity studies in rats were usually evaluated for cholinesterase inhibition; neurobehavioral effects (Functional Observational Battery); and histopathology of the central and peripheral nervous system following single or repeated exposures.

All of the organophosphates are neurotoxic in that they may cause cholinesterase inhibition and related clinical signs, up to and including death following exposure. Organophosphates also may cause neuropathology of the visual system or effects on cognitive function, i.e., learning and memory as well as other effects on the nervous system. While acute and subchronic neurotoxicity studies may show some gross effects on the visual system or sensory function, these and other effects were not systematically evaluated at this meeting since the cause and effect relationship between cholinesterase inhibition and visual system effects has not been verified.

Of the 34 organophosphates that had neurotoxicity studies available, evidence of neuropathology was seen for the following:

CHEMICAL	EVIDENCE OF NEUROPATHOLOGY
Chlorpyrifos	Published studies have reported OPIDN in humans and animals (at lethal doses) and there have been case reports that indicate possible correlation of neurophysiological effects in humans.
Methamidophos	Positive neurotoxic esterase in a subchronic toxicity study in hens and delayed peripheral neuropathy in humans as well as polyneuropathy in hens at extremely high dose levels (greatly in excess of the hen LD_{50}) reported in published studies.
Methyl Parathion	Neuropathology in acute and subchronic neurotoxicity studies in rats and the chronic toxicity studies in rats.
Naled	In an acute delayed neurotoxicity study, axonal degeneration of the spinal cord was seen following a single oral dose. However, no neuropathy was seen after repeated dosing in the subchronic neurotoxicity study in hens. No evidence of neuropathology was seen following single or repeated dosing in rats.
ODM	Evidence of neuropathology was seen in hens following a single dose but no neuropathology was seen following repeated dose in hens. No evidence of neuropathology was seen following single or repeated dosing in rats.
Tribuphos	Evidence of OPIDN and neuropathology following repeated dermal applications in a subchronic delayed neurotoxicity study in hens.
Trichlorfon	Evidence of OPIDN and neuropathology in the acute delayed neurotoxicity study in hens and neuropathology in the subchronic neurotoxicity study in hens.

A study that evaluates the effects on the NTE is necessary for the following chemicals. The lack of NTE data in an otherwise acceptable negative hen study is not considered a major data gap, but indicates a need for confirmatory data (i.e., data to confirm that an effect on NTE does not occur).

ORGANOPHOSPHATES THAT REQUIRE ASSESSMENT OF NTE				
Azinphos-Methyl Ethion Methidathion Profenophos Trichlorfon	Cadusafos[1] Ethoprop Methyl Parathion Propetamphos	Coumaphos Fenitrothion Phorate Terbufos	Dimethoate Fenamiphos Phostebupirim Tetrachlorvinphos	Disulfuton[1] Isofenphos Pirimiphos-Methyl[1] Tribuphos

[1] Data gap exists for an acute delayed neurotoxicity study for these four chemicals.

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2. Determination of Susceptibility

The HIARC evaluated the potential for enhanced susceptibility from exposure to these pesticides as required by the FQPA. This evaluation entailed the enhanced susceptibility of fetuses as compared to maternal animals following *in utero* exposure in rats and rabbits, as well as the enhanced susceptibility of pups as compared to adults in the two-generation toxicity study in rats. For most of these pesticides, following *in utero* exposures, developmental effects were observed at or above treatment levels which resulted in evidence of maternal toxicity. Following pre- and/or postnatal exposure in the two-generation reproduction toxicity study, in general, effects in the offspring were most often manifested as decreased pup viability at doses that caused considerable inhibition of cholinesterase activity and cholinergic signs in the parental animals. Since the effects seen in the offspring (e.g., decreased pup viability) are confounded by the presence of maternal toxicity, it is difficult to regard the offspring effects as indicative of developmental toxicity or enhanced susceptibility of young animals. In addition, in the prenatal developmental toxicity studies, the parameters evaluated are not comparable between the dams and the fetuses. While the dams are routinely evaluated for survival, clinical signs, body weight, body weight gain, food consumption, and certain reproductive parameters during the cesarian section, the fetuses undergo much more critical and more detailed evaluation. Therefore, the HIARC conducted a qualitative evaluation of the effects seen in the fetuses and/or pups as compared to the maternal/parental effects in order to ascertain whether the fetal/offspring effects were true indicators of susceptibility.

The primary effect for the organophosphates is the inhibition of cholinesterase activity. For most of the pesticides, however, comparative cholinesterase inhibition data for the dams and the pups were not available, thus precluding an evaluation of susceptibility based on this endpoint. When these data (i.e., comparative cholinesterase) were available however, no evidence of enhanced susceptibility was seen in the pups as compared to maternal animals (i.e., cholinesterase inhibition occurred at the same doses in the pups and parental animals).

i. Prenatal Developmental Toxicity Study in Rats

(a) The NOELs, LOELs, and endpoints selected for maternal and developmental toxicity in the prenatal developmental toxicity studies in rats are provided in **Attachment 1**. No evidence of enhanced susceptibility was observed for 33 of 40 organophosphates following *in utero* exposure to pregnant rats. For these chemicals, there was no evidence of developmental effects being produced in fetuses at lower doses as compared to maternal animals, nor was there evidence of an increase in severity of effects at or below maternally toxic doses. Of the remaining 7: an acceptable prenatal developmental toxicity study in rats was not available for Chlorpyrifos-methyl, Dicrotophos, Temephos, and

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Trichlorfon; and no data were available for Fonofos, Isazophos, and Sulfotepp. It is noted that in pre/postnatal studies published in the open literature, evidence of enhanced susceptibility was demonstrated in rats for Chlorpyrifos following oral, subcutaneous and intraperitoneal administration and for Methyl Parathion via the subcutaneous, and intraperitoneal routes.

(b) For four chemicals (tabulated below), the NOELs and LOELs were the same for maternal and developmental toxicity (i.e., fetal effects were seen at the same dose that caused maternal toxicity) but the developmental (fetal) effects initially appeared to be more severe. Following a qualitative re-evaluation of the effects observed, the HIARC concluded that fetal effects occurred at dose levels causing similar or more severe maternal toxicity. The rationale for this conclusion is provided for each chemical.

DEVELOPMENTAL TOXICITY IN THE PRESENCE OF MATERNAL TOXICITY (DEVELOPMENTAL TOXICITY STUDIES-RATS)	
Cadusafos	Decreased fetal body weights occurred at levels causing cholinergic signs in the dams characterized as tremors, muscle fasciculations, exophthalmus and decreased activity.
Fenthion	Increased post-implantation losses were not accompanied by decreased litter sizes and no developmental effects were seen in the other parameters examined. Dams exhibited clinical signs and decreased body weights at the same dose that induced fetal effects. In addition, plasma, erythrocyte, and brain cholinesterase inhibition was seen in dams at doses lower than those causing fetal effects indicating that the dams were under stress.
Fenitrothion	There was an increased incidence of fetuses with skeletal variations at a dose that caused severe maternal toxicity, characterized as tremors and decreases in body weight and body weight gains.
Terbufos	The biological significance of the fetal effects (increases in early fetal resorptions and postimplantation losses) are questionable since similar effects (i.e., decreased litter size) were not seen in the two-generation study in rats. In addition, based on the results of other studies with this chemical, substantial cholinesterase inhibition may have occurred in dams (not measured in this study) and thus most likely contributed to the fetal effects.

ii. **Prenatal Developmental Toxicity Study in Rabbits**

(a) The NOELs, LOELs, and endpoints selected for the maternal and developmental toxicity in the prenatal developmental toxicity study in rabbits are provided in **Attachment 2.** No evidence of enhanced susceptibility was observed for 34 of 40 organophosphates following *in utero* exposure to pregnant rabbits. For these chemicals, there was no evidence of developmental effects being produced in fetuses at lower doses as compared to maternal animals nor was there evidence of an increase in severity of effects at or below maternally toxic doses. Of the remaining 6, an acceptable prenatal developmental toxicity study in rabbits was not available for Chlorpyrifos-methyl, Dicrotophos, and Temephos, and no data was available for Fonofos, Isazophos, and Sulfotepp.

(b) For five chemicals (tabulated below), the NOELs and LOELs were the same for maternal and developmental toxicity (i.e., fetal effects were seen at the same dose that caused maternal toxicity) but the developmental (fetal) effects appeared to be more severe. Following a qualitative evaluation of the effects observed, the HIARC concluded that fetal effects occurred at dose levels causing similar or more severe maternal toxicity. The rationale for this conclusion is provided for each chemical.

DEVELOPMENTAL TOXICITY IN THE PRESENCE OF MATERNAL TOXICITY (DEVELOPMENTAL TOXICITY STUDIES-RABBITS)	
Cadusafos	Severe maternal toxicity manifested as increased mortality and cholinergic signs at the same dose that caused an increase in total number of resorptions, decrease in total number of fetuses, and fetal death.
Ethyl Parathion	The dose that caused maternal deaths, increased moribundity, as well as decreases in body weight and body weight gains also caused a decrease in litter size.
Malathion	The slight increase in mean resorption sites was not accompanied by alteration in litter size and occurred at the same doses that caused decreased maternal body weights.
Phosmet	The dose that induced clinical signs and decreased body weight in dams, also resulted in skeletal variations observed in the fetuses.
Propetamphos	The increased resorptions were not accompanied by decreases in litter size.

iii. **Two-Generation Reproduction Study in Rats**

(a) The NOELs, LOELs, and endpoints selected for the parental systemic and offspring toxicity in the two-generation reproduction study is provided in **Attachment 3.** No evidence of enhanced susceptibility was observed for

35 of 40 organophosphates following pre and/or post natal exposure in the two-generation reproduction study in rats (i.e., effects noted in offspring occurred at maternally toxic doses or higher). Of the remaining 5, an acceptable reproduction toxicity study in rats was not available for Chlorpyrifos-methyl, and Temephos, and no data were available for Fonofos, Isazophos, and Sulfotepp.

(b) For the following chemicals, the NOELs and LOELs were same for parental systemic toxicity and offspring toxicity (i.e., offspring effects were seen at the same dose that caused parental effects) but the offspring (pup) effects initially appeared to be more severe. Following a qualitative reevaluation of the effects observed, the HIARC concluded that the effects in the pups occurred at dose levels causing similar or more severe parental systemic toxicity. The rationale for this conclusion is provided for each chemical.

OFFSPRING TOXICITY IN THE PRESENCE OF PARENTAL TOXICITY (MULTIGENERATION REPRODUCTION TOXICITY STUDIES-RATS)	
Acephate	Decreased viability index and decreased pup body weight gain were seen at the same dose that caused parental toxicity characterized by clinical signs (alopecia and soft stools) and decreased body weight gain. Although the clinical signs in parental animals are not severe, comparison to other studies (subchronic) indicated that cholinesterase inhibition (not measured in this study) would have occurred in dams at the dose that caused offspring toxicity and thus most likely contributed to offspring toxicity. Also, the offspring effects were seen in the first generation only and not repeated in the second generation (i.e., not a consistent finding).
Dichlorvos	The abnormal estrous cycles observed in maternal animals most likely contributed to the offspring effects (reduced dams bearing litters, decreases in fertility and pregnancy indices) observed at the same dose.
Diazinon	Cholinesterase inhibition (ChEI) was not measure in parental animals in the reproduction study. ChEI was, however, was observed at lower doses in the other toxicity studies. Therefore it is postulated that ChEI occurred in the maternal animals at the same doses causing pup mortality and decreased pup weight gain observed during lactation at which time the pups were exposed to the chemical via the milk.

OFFSPRING TOXICITY IN THE PRESENCE OF PARENTAL TOXICITY (MULTIGENERATION REPRODUCTION TOXICITY STUDIES-RATS)	
Fenitrothion	The dose that caused severe parental systemic toxicity (decreases in body weight and body weight gain as well as food consumption) was also associated with offspring toxicity (decreases in fertility index, number of implantation sites and viability) in one generation. However, similar offspring toxicity was not seen in the second generation (i.e., not replicated in the second generation).
Isofenphos	Offspring toxicity manifested as increased pup mortality (reductions in lactation indices and mean litter size) and clinical signs (small to very small emaciated pups) were observed at the same dose that caused parental systemic toxicity (inhibition of plasma, erythrocyte and brain cholinesterase). The offspring toxicity was not considered to be more severe since: 1) the effects were observed only after postnatal Day 14 and not on other days (i.e., a single occurrence) and thus the biological significance is not known; 2) during that period (i.e., later portion of lactation), young rats consume approximately twice the diet per unit body weight as an adult rat consumes. Estimation of the test substance intake in pre-weaning animals is likely to be more than double the adult intake because of the availability of the test material both via the milk (lactation) and food, particularly after the mid point of lactation; and 3) the dose that caused the offspring toxicity also caused cholinesterase inhibition (all three compartments) in parental animals.
Malathion	The decreases in the F1a and F2b pup body weight occurred at a lower dose than the dose that caused parental toxicity; this was not a true indication of enhanced susceptibility because: 1) pup body weight decrements were primarily observed at postnatal Day 21; 2) during that period, young rats consume approximately twice the diet per unit body weight as an adult rat consumes; and 3) the estimation of the test substance intake in pre-weaning animals is likely to be more than double the adult intake because of the availability of the test material both via the milk (lactation) and food, particularly after the mid point of lactation.
Methamidophos	Substantial cholinesterase inhibition was seen at lower doses in other toxicity studies conducted with rats indicating that cholinesterase inhibition most likely occurred in parental animals at a dose that caused offspring toxicity (decreased pup viability). Also this effect was seen only on postnatal Day 14 and only in one generation. It is noted that decreased pup viability was also seen with Acephate, a related organophosphate, at the same dose that caused parental toxicity.

OFFSPRING TOXICITY IN THE PRESENCE OF PARENTAL TOXICITY (MULTIGENERATION REPRODUCTION TOXICITY STUDIES-RATS)	
Oxydemeton-methyl (ODM)	The same dose that caused cholinesterase inhibition in parental animals also caused offspring toxicity (decreased viability index, decreased litter size at birth, and decreased pup body weight gain during lactation). In addition, no enhanced susceptibility was seen in adults vs. fetuses based on comparative cholinesterase inhibition data (i.e., cholinesterase inhibition occurred at the same doses in the pups and the parental animals).
Phorate	The same dose that caused severe parental toxicity (tremors and inhibition of plasma and brain cholinesterase activity) also caused decreased pup survival and pup body weight.

3. Summary of the Hazard Assessments

The HIARC's assessments for neurotoxicity, enhanced susceptibility, the need for additional data, or the requirement of a developmental neurotoxicity study is summarized in **Attachment 4**.

III. EXPOSURE ASSESSMENT

1. Dietary Exposure

i. Considerations

Dietary exposure assessment addresses the potential for exposure to infants and children from pesticide residues in food. Considerations include: the evaluation of use patterns; actual dietary consumption and exposure data or estimates; and the completeness of the data, including characterization of uncertainties pertaining to dietary exposure.

For each pesticide, the following information was evaluated (as available):

- Whether the pesticide has major agricultural uses.
- Range of application rates and frequency of applications.
- Range of established tolerances and the nature of the metabolites requiring regulation.
- Whether the pesticide is used on commodities preferentially consumed by infants and children (such as citrus fruit, pome fruit, cereal grains, milk, soybeans, etc.); and if so, which ones.
- Whether the pesticide is "systemic", indicating residues are distributed throughout the commodity and not likely to be removed by preparation such as washing or peeling.

- Available residue data sources for the pesticide (field studies, FDA monitoring data, PDP monitoring data, etc.).
- Brief description of the range and frequency of positive residue findings for the pesticide.
- Extent of possible refinement to the Dietary Risk Evaluation System (DRES) analyses (ie., tolerance levels, anticipated residues (ARs), percent crop treated (%CT), monitoring data, Monte Carlo distributional analysis, etc.).
-

ii. Summary of Dietary Exposure Assessments

A summary table of the considerations used in the dietary exposure assessments for each of the OPs is presented in **Attachment 5**. This information was obtained from the HED Reregistration Eligibility Document (RED) Chapters or executive summaries of the HED RED Chapter, Dietary Risk Evaluation System (DRES) analyses reports, and/or risk characterization summaries.

2. Drinking Water Exposure

i. Considerations

Drinking water exposure assessment addresses the potential for exposure to infants and children from contaminated water sources. Considerations include: actual exposure data or estimates; the completeness of the environmental fate data, including characterization of uncertainties, as well as the evaluation of the use patterns pertaining to drinking water exposure.

For each pesticide, the following information was evaluated (as available):

- Completeness of the environmental fate data base.
- Whether the compound or its degradate(s) has the potential to leach to drinking water sources.
- Whether ground and/or surface water studies (or other appropriate, reliable, targeted monitoring data) were used to calculate estimated environmental concentrations (EECs) for the pesticide; and if so, whether the studies were conducted in vulnerable areas at maximum label rates.
- Whether ground water and surface water EECs were based on modeling; and if so, the model and tier used.
- Description of the extent of exposure and the potential population affected.

ii. Summary of Drinking Water Exposure Assessments

A summary table of the considerations used in the drinking water exposure assessments for each of the OPs is presented in **Attachment 6**. This information was obtained from the HED Reregistration Eligibility Document (RED) Chapters

or executive summaries of the HED RED Chapter, EFED Drinking Water Assessment reports, and/or risk characterization summaries.

3. Residential Exposure

i. Considerations

Residential exposure assessment addresses the potential for exposure to infants and children from non-dietary, non-occupational sources. Considerations include: the evaluation of use patterns; actual exposure data or estimates; and the completeness of the data, including characterization of uncertainties pertaining to residential exposure.

For each pesticide, the following information was evaluated (as available):

- Whether infants and children could be exposed from the use of the pesticide.
- Whether pesticide-specific or site-specific data are available for the exposure assessment.
- Whether Pesticide Handler Exposure Data base (PHED) data is used; and if so, whether the scenarios used reflect the actual use pattern.
- Whether the *Draft Standard Operating Procedures for Residential Exposure Assessments* were used as the basis for post-application exposure calculations; and if so, a description of any deviations from SOP calculations.
- Whether other models were used; and if so, the model and tier used.
- Whether any biological exposure or epidemiology data are available (e.g., incident reports, CDC monitoring data, etc.); and if so, a description of the data.
- Whether 100% dermal absorption is assumed in the exposure assessment when dermal endpoints are derived from oral studies.

ii. Summary of Residential Exposure Assessments

A summary table of the considerations used in the residential exposure assessments for each of the OPs is presented in **Attachment 7.** This information was obtained from the HED Reregistration Eligibility Document (RED) Chapters or executive summaries of the HED RED Chapter, and/or risk characterization summaries.

IV. FQPA SAFETY FACTOR RECOMMENDATION AND RATIONALE

In determining whether to recommend removal, reduction, or retention of the FQPA safety factor for each of the organophosphates, the Committee considered: 1) the hazard and dose response evaluations; 2) the exposure assessment(s); and 3) the characterization of both the hazard and exposure data base.

1. Recommendations for the FQPA Safety Factor

The FQPA Safety Factors recommended by the FQPA Safety Factor Committee are presented below:

Removed (1x)	Reduced to 3x	Retained (10x)
Acephate Azinphos-methyl Bensulide Chlorethoxyfos Diazinon Dimethoate Ethion Ethoprop Ethyl Parathion Fenamiphos Fenitrothion Fenthion Malathion Methidathion Naled Profenofos Propetamphos Tetrachlorvinphos	Coumaphos Dichlorvos (DDVP) Disulfoton Isofenphos Methamidophos Phorate Phosmet Phostebupirim Pirimiphos-methyl Terbufos	Cadusafos Chlorpyrifos Methyl parathion Oxydemeton-methyl Tribuphos (DEF) Trichlorfon

Retained (10x) - Inadequate Tox Data base	Other
Chlorpyrifos-methyl Dicrotophos Temephos	Fonofos: cancellation proceedings are in place. Isazophos-methyl: no toxicology or exposure data are available for an adequate assessment. Sulfotepp: FQPA not applicable (greenhouse use only).

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2. Rationale for the Recommendations for the FQPA Safety Factor

i. FQPA Safety Factor Removed (1x)

For **Acephate, Azinphos-methyl, Bensulide, Chlorethoxyfos, Diazinon, Dimethoate, Ethion, Ethoprop, Ethyl Parathion, Fenamiphos, Fenthion, Fenitrothion, Malathion, Methidathion, Naled, Profenofos, Propetamphos, and Tetrachlorvinphos** the FQPA safety factor is **removed** based on the following factors:

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

(b) In the pre/post natal two-generation reproduction study in rats, there was no evidence of enhanced susceptibility in pup when compared to adults (i.e., effects noted in offspring occurred at maternally toxic doses or higher).

(c) There was no evidence of abnormalities in the development of the fetal nervous system in the pre/post natal studies.

(d) There is no concern for positive neurological effects from the available neurotoxicity studies or for histopathology in the central nervous system from the other toxicological studies (e.g., subchronic rat, chronic dog, chronic mouse and rat).

(e) The toxicology data base is complete and there are no data gaps according to the Subdivision F Guideline requirements.

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

ii. FQPA Safety Factor Reduced (3x)

For **Coumaphos, Dichlorvos, Disulfoton, Isofenphos, Methamidophos, Phorate, Phosmet, Phostebupirim, Pirimiphos-methyl, and Terbufos** the FQPA safety factor is **reduced to 3x.**

In general, the hazard (based on the neurotoxicity, developmental and reproductive toxicity studies) and exposure (dietary, drinking water and residential) assessments for these ten pesticides indicate the following:

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

(b) In the pre/post natal two-generation reproduction study in rats, there was no evidence of enhanced susceptibility in pups when compared to adults (i.e., effects noted in offspring occurred at maternally toxic doses or higher).

(c) There was no evidence of abnormalities in the development of the fetal nervous system in the pre/post natal studies.

(d) There is no concern for positive neurological effects from the available neurotoxicity studies or for histopathology in the central nervous system from the other toxicological studies (e.g., subchronic rat, chronic dog, chronic mouse and rat studies).

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

However, there were partial data gaps for the neurotoxicity studies (7 pesticides) and evidence of neuropathology (2 pesticides) which led to either requiring or reserving the requirement for a developmental neurotoxicity study for these pesticides (9 total). When a developmental neurotoxicity study is required, it is because this study will provide additional data (e.g., potential increased susceptibility, effects on the development of the fetal nervous system, etc.). When the requirement for a developmental neurotoxicity study is placed in reserve status, the Agency will make the final requirement decision following evaluation of the results of the neurotoxicity studies (i.e., data gaps). For one pesticide there was concern for decreased brain weights in guinea pig fetuses as reported in the open literature, as well as uncertainty in the chemical specific residential exposure data.

Therefore, the Committee determined that a FQPA safety factor was necessary for these pesticides. However, it was determined that the 10x factor can be reduced to 3 x and the rationale is provided below:

> Specifically, for **Coumaphos, Disulfoton, Phorate, Phosmet, Phostebupirim, Pirimiphos-methyl, and Terbufos** the FQPA safety factor is **reduced to 3x** because of data gaps for one of the neurotoxicity studies (i.e., acute delayed neurotoxicity-hen and/or acute or subchronic-rat) and the requirement for a developmental neurotoxicity study placed in reserve status. The results of these neurotoxicity studies may "trigger" the requirement of a developmental neurotoxicity study which in turn will provide additional data (e.g., potential increased susceptibility, effects on the development of the fetal nervous system, etc.).

For **Methamidophos** and **Isofenphos** there was evidence of neuropathology reported in the open literature indicating that an FQPA safety factor is appropriate. The Committee, however, determined that the 10x factor can be **reduced to 3x** because: 1) there was no increased susceptibility seen in studies submitted to the Agency, 2) there was no evidence of abnormalities in the development of the fetal nervous system in the pre/post natal studies, 3) there were no positive neurological effects in other toxicology studies; 4) the toxicology data base is complete; and 5) no concern is indicated by exposure assessment.

> Specifically for **Methamidophos,** polyneuropathy was observed in hens at high doses, as well as the occurrence of delayed peripheral neuropathy in humans (through accidental occupational poisoning, suicide attempts, or ingestion of contaminated vegetables) as reported in the open literature.
>
> Specifically for **Isofenphos,** delayed neuropathy was observed in an agricultural worker exposed to multiple pesticides including Isofenphos (as reported in the open literature), as well as concern for a number of poisoning incidents involving children (ages ≤ 5) reported by the Poison Control Center (1985-92 data).

For both pesticides, these concerns "triggered" the requirement for a developmental neurotoxicity study which in turn will provide additional data (e.g., potential increased susceptibility, effects on the development of the fetal nervous system, etc.). For Isofenphos, the developmental neurotoxicity study was requested by the FQPA Safety Factor Committee.

Specifically for **Dichlorvos (DDVP),** decreased brain weights in guinea pig fetuses was reported in the open literature. Additionally, there is concern for uncertainty in the chemical specific residential exposure data which warrants the FQPA safety factor. The Committee, however, determined that the 10x factor can be **reduced to 3x** because: 1) there was no increased susceptibility seen in studies submitted to the Agency, 2) there was no evidence of abnormalities in the development of the fetal nervous system in pre/postnatal studies or concern for positive neurological effects in other toxicology studies; and 3) the toxicology data base is complete.

In addition, the HIARC determined that a prenatal developmental toxicity study in guinea pigs is necessary to confirm the findings of the literature study; and therefore, the requirement of developmental neurotoxicity study is placed in reserve status pending the results of the aforementioned study.

iii. FQPA Safety Factor Retained (10x)

For **Cadusafos, Chlorpyrifos, Methyl Parathion, Oxydemeton-methyl, Tribuphos and Trichlorfon**, the FQPA safety factor of **10x** is **retained.**

The reasons for retaining the FQPA safety factor (10x) are based on: data gaps for all three neurotoxicity studies (1 pesticide); evidence of increased susceptibility (2 pesticides); concern for heritable effects (1 pesticide); evidence of neuropathology, as well as data gaps for neurotoxicity studies (1 pesticide); and

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evidence of neuropathology, data gaps for neurotoxicity and prenatal developmental toxicity studies (1 pesticide).

In general, hazard (based on the neurotoxicity, developmental, and reproductive toxicity studies) and exposure (dietary, drinking water, and residential) assessments indicate:

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

(b) In the pre/post natal two-generation reproduction study in rats, there was no evidence of enhanced susceptibility in pup when compared to adults (i.e., effects noted in offspring occurred at maternally toxic doses or higher).

(c) There was no evidence of abnormalities in the development of the fetal nervous system in the pre/post natal studies submitted to the Agency.

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

Specifically for **Cadusafos,** there are data gaps for all three neurotoxicity studies (i.e., acute delayed in hens as well as acute and subchronic studies in rats) which places the requirement of a developmental neurotoxicity study in reserve status.

Specifically for **Chlorpyrifos** and **Methyl parathion,** in studies conducted at various scientific laboratories and reported in the open literature, neuropathology was observed in animals and/or humans, and evidence of increased susceptibility was seen in prenatal developmental toxicity studies in rats following oral, subcutaneous and/or intraperitoneal administrations. Although the subcutaneous and intraperitoneal routes of exposure are not traditional (i.e., oral), the Committee determined that the demonstration of increased susceptibility, as well as occurrence of neuropathology warrants the 10x safety factor. Also, these concerns result in the requirement of a developmental neurotoxicity study for both of these pesticides. *Note: The Agency acknowledges the recent receipt of a developmental neurotoxicity study for Chlorpyrifos which is currently under review.*

Specifically for **Oxydemeton methyl** there is concern for heritable effects as demonstrated in an *in vivo* mouse spot test. This test was positive for the induction of somatic cell mutations following intrauterine exposure of embryos. This adverse effect is clearly associated with the developing embryos thus warranting the 10x safety factor. A reproducible, concentration-dependent increase in mutation was seen at doses lower than the level causing maternal toxicity. In addition, there was valid evidence of DNA strand breaks in rat testes cells in an *in vitro* alkaline elution assay (not confirmed *in vivo*). Based on these

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concerns, the HIARC required a mouse specific locus test (this requirement was "triggered"by the positive mouse spot test).

Specifically for **Tribuphos,** OPIDN and neuropathology was observed following repeated dermal applications in hens, ocular effects and neuropathology were also seen in several species. In addition, there are data gaps for all three neurotoxicity studies. The concern for the effects seen after dermal exposure, in conjunction with the data gaps resulted in the requirement of a developmental neurotoxicity study.

Specifically for **Trichlorfon,** the safety factor is retained based on a number of factors including occurrence of neuropathology, as well as the presence of data gaps. Neurotoxicity concerns include the presence of OPIDN and neuropathology in hens, as well as decrease in brain weights in guinea pig fetuses in a prenatal developmental toxicity study identified in open literature. Data gaps include acute and subchronic neurotoxicity studies in rats and a prenatal developmental toxicity study in rats. These factors resulted in the requirement of a prenatal developmental toxicity study in guinea pigs (to verify the findings reported in the open literature). The developmental neurotoxicity study in rats is placed in reserve status pending the results of the developmental toxicity study in the guinea pigs.

For **Chlorpyrifos-methyl, Dicrotophos, and Temephos** the FQPA safety factor is **retained** solely because of the inadequacy of the toxicology data base which precluded an evaluation of potential enhanced susceptibility to infants and children.

iv. FQPA Safety Factor Not Determined

An FQPA safety factor could not be determined for: **Fonofos**, since cancellation proceedings are in place for this pesticide; and **Isazophos-methyl**, for which there are no toxicology or exposure data available.

v. FQPA Safety Factor Not Applicable

An FQPA safety factor is not applicable to **Sulfotepp** since the only registered use is for greenhouses and there is no potential for exposure via the dietary, drinking water, or residential routes.

3. Application of the FQPA Safety Factor

For most of the organophosphates, the FQPA safety factor recommendations result from datagaps in the toxicology data requirements. The lack of a complete database encompasses the general population and is not limited to any one subpopulation.

For those organophosphates that require a developmental neurotoxicity study, the results from this study may be used in selecting endpoints that are applicable to risk assessments for all population groups.

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When a developmental neurotoxicity study is required, it is generally recognized that the developmental effects seen in this study are considered to be "acute" effects and thus relevant for acute dietary risk assessment since it is presumed that developmental effects may arise from a single exposure. However, the results from this study may also be applicable for chronic dietary risk assessments because: 1) an extended dosing regimen (day 6 of gestation to day 10 postnatal) is used in the study; 2) developmental effects can occur at doses lower than those that induce chronic effects; and 3) adverse effects on human development can occur from birth through adolescence (long term process). Thus, the uncertainty related to the absence of a developmental neurotoxicity study makes it appropriate to apply a FQPA safety factor for acute and chronic dietary and non-dietary risk assessments for the general population including infants and children.

The FQPA safety factors are relevant for acute and chronic dietary risk assessments since the endpoints are based on plasma, red blood cell, and/or brain cholinesterase inhibition seen following single (acute) and/or repeated (chronic) exposures. Furthermore, it is also applied when performing residential (dermal and inhalation) exposure risk assessments, which utilize the oral endpoints with appropriate absorption factors for route-to-route extrapolation.

V. COMBINED UNCERTAINTY FACTORS FOR RISK ASSESSMENT

In risk assessment calculations, the FQPA safety factor recommendations must be considered along with the conventional Uncertainty Factors (i.e., 10x for interspecies extrapolation and 10x for intraspecies variability), and any additional Uncertainty Factors (UFs) assigned by the HIARC for various toxicological considerations. Examples of such considerations include the use of a LOEL when a NOEL was not established in the critical study or the use of a single sex human study. Presented below are the conventional Uncertainty Factors, the additional Uncertainty Factors assigned as needed by HIARC, the FQPA safety factor, and the resulting combined factors.

PESTICIDE	EXPOSURE SCENARIO	CONVEN-TIONAL FACTOR	ADDITIONAL UNCERTAINTY FACTOR (REASONS)	FQPA FACTOR	COMBINED FACTOR
Acephate	All[1]	100	No additional factor required	1	100
Azinphos-methyl	Acute Chronic No residential uses	100 100	3 (use of LOEL) No additional factor required	1	300 100
Bensulide	All	100	No additional factor required	1	100

[1] "All" indicates acute dietary, chronic dietary, and residential exposure scenarios.

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PESTICIDE	EXPOSURE SCENARIO	CONVEN-TIONAL FACTOR	ADDITIONAL UNCERTAINTY FACTOR (REASONS)	FQPA FACTOR	COMBINED FACTOR
Cadusafos	Acute Chronic No residential uses	100	No additional factor required	10	1000
Chlor-ethoxyfos	Acute Chronic No residential uses	100	No additional factor required	1	100
Chlorpyrifos	All	10	No additional factor required	10	100
Coumaphos	Acute Chronic No residential uses	100	No additional factor required	3	300
Diazinon	Acute Chronic Residential, Dermal[2] Residential, Inhalation[3]	100 10 10 100	No additional factor required 3 (NOEL/LOEL and one sex) [4] 3 (NOEL/LOEL and one sex) 3 (use of a LOEL)	1	100 30 30 300
Dimethoate	All	100	No additional factor required	1	100
Disulfoton	All	100	No additional factor required	3	300
DDVP	Acute Chronic Residential: Short-Term, dermal Intermediate, dermal Long-Term, dermal Inhalation	10 100 10 10 NA 100	No additional factor required No additional factor required No additional factor required 3 (use of a LOEL) Not required/No use No additional factor required	3	30 300 30 100 NA 300

[2] For all time periods (Short-, Intermediate-, and Long-Term) unless otherwise stated.

[3] For all time periods (Short-, Intermediate-, and Long-Term) unless otherwise stated.

[4] Diazinon: closeness of NOEL/LOEL established in the study.

PESTICIDE	EXPOSURE SCENARIO	CONVEN-TIONAL FACTOR	ADDITIONAL UNCERTAINTY FACTOR (REASONS)	FQPA FACTOR	COMBINED FACTOR
Ethion	Acute Chronic No residential uses	10 10	No additional factor required 10 (use of a LOEL and other reasons)[5]	1	10 100
Ethoprop	Acute Chronic No residential uses	100	No additional factor required	1	100
Ethyl parathion	Acute Chronic No residential uses	100 100	No additional factor required 3 (use of a LOEL)	1	100 300
Fenamiphos	Acute Chronic No residential uses	100 100	3 (use of a LOEL) No additional factor required	1	300 100
Fenitrothion	All	100	No additional factor required	1	100
Fenthion	Acute Chronic No residential uses	10 10	No additional factor required 3(threshold NOEL/LOEL)	1	10 30
Isofenphos	Acute Chronic Residential, Dermal and Inhalation: Short-Term Intermediate and Long-Term	100 100 100 100	3 (use of a LOEL) No additional factor required 3 (use of a LOEL) No additional factor required	3	1000 300 1000 300
Malathion	Acute Chronic Residential: Dermal (all time periods) Inhalation, Short-Term Intermediate and Long-Term	100 100 100 100 100	No additional factor required No additional factor required No additional factor required No additional factor required 3 (use of a LOEL)	1	100 100 100 100 300

[5] A UF of 10 was necessary due to the lack of a NOEL in the critical (human) study and the possibility that brain cholinesterase could be inhibited at dose levels comparable to those causing plasma cholinesterase inhibition as demonstrated in animal studies.

PESTICIDE	EXPOSURE SCENARIO	CONVEN -TIONAL FACTOR	ADDITIONAL UNCERTAINTY FACTOR (REASONS)	FQPA FACTOR	COMBINED FACTOR
Metho-midophos	Acute Chronic No residential uses	100	No additional factor required	3	300
Methidathion	Acute Chronic No residential uses	100	No additional factor required	1	100
Methyl parathion	Acute Chronic No residential uses	100	No additional factor required	10	1000
Naled	All	100	No additional factor required	1	100
Oxydemeton-methyl	Acute Chronic No residential uses	100 10	3 (use of a LOEL) No additional factor required	10	3000 100
Phorate	Acute Chronic No residential uses	100	No additional factor required	3	300
Phosmet	All	100	No additional factor required	3	300
Phostebupirim	Acute Chronic No residential uses	100	No additional factor required	3	300
Pirimiphos-methyl	Acute Chronic No residential uses	10 10	No additional factor required 30 (use of a LOEL + data gaps) [6]	3	30 1000
Profenofos	Acute Chronic No residential uses	100	No additional factor required	1	100
Propetamphos	All	100	No additional factor required	1	100
Terbufos	Acute Chronic No residential uses	100	No additional factor required	3	300
Tetra-chlorvinphos	All	100	No additional factor required	1	100

[6] Pirimiphos-methyl: Data gaps exists for a chronic toxicity study in dogs and a chronic/carcinogenicity study in rats.

PESTICIDE	EXPOSURE SCENARIO	CONVEN -TIONAL FACTOR	ADDITIONAL UNCERTAINTY FACTOR (REASONS)	FQPA FACTOR	COMBINED FACTOR
Tribuphos	Acute Chronic No residential uses	100 100	No additional factor required No additional factor required	10	1000 1000
Trichlorfon	Acute Chronic Residential	10 100 100	No additional factor required No additional factor required No additional factor required	10	100 1000 1000

ATTACHMENT 1

NOELs/LOELs and ENDPOINTS FOR DEVELOPMENTAL TOXICITY STUDIES IN RATS

ATTACHMENT 1. NOELs/LOELs & ENDPOINTS FOR DEVELOPMENTAL TOXICITY STUDIES IN RATS						
CHEMICAL	MATERNAL TOXICITY			DEVELOPMENTAL TOXICITY		
	(mg/kg/day)		ENDPOINT	(mg/kg/day)		ENDPOINT
	NOEL	LOEL		NOEL	LOEL	
1) ACEPHATE	5.0	20.0	Decreases in body weight, body weight gain, food consumption and food efficiency.	20.0	75.0	Decrease in mean number of ossification on center/litter
2) AZINPHOS METHYL	0.5	1.0	RBC & Brain ChEI	≥2.0	(NA)	No developmental toxicity at HDT.
3) BENSULIDE	23.0	95.0	Clinical sign (tremors), decreases in body weight and body weight gain/food consumption and increased relative liver weights.	≥95.0	NA	No developmental toxicity at HDT.
4) CADUSAFOS	6	18	Cholinergic signs (decreased locomotion, tremors, exothalomus, fasciculation).	6	18	Decreased fetal body weight.
5) CHLORETHOXYFOS	0.25	0.25	Decrease body weight.	NA	50	Delayed ossification of sternebrae.
6) CHLORPYRIFOS	0.1	3.0	Plasma & RBC ChEI.	≥15.0	NA	No developmental toxicity at HDT.
	0.5	2.5	Decreased body weight and food consumption.	2.5	15.0	Increased post implantation loss.
7) CHLORPYRIFOS METHYL	100	200	**STUDY UNACCEPTABLE**	≥200	NA	**STUDY UNACCEPTABLE**
8) COUMAPHOS	5	25	Clinical signs of cholinesterase inhibition.	25	NA	No developmental toxicity at HDT.
9) DICHLORVOS (DDVP)	3	21	Cholinergic signs (Tremors, hind leg splay, vocalization, prone positioning).	NA	21	No developmental toxicity at HDT.
10) DIAZINON	20	100	Decreased body weight, body weight gain and food consumption.	≥100	NA	No developmental toxicity at HDT.
11) DICROTOPHOS	0.5	1.0	Clinical signs (Fasiculations)	≥2.0	NA	No developmental toxicity at HDT
12) DIMETHOATE	3.0	6.0	Small pellet like feces.	≥18.0	NA	No developmental toxicity at HDT.
13) DISULFOTON	0.1	0.3	Plasma and RBC ChEI.	0.3	1.0	Incomplete ossification of intraparietals and sternebrae

ATTACHMENT 1. NOELs/LOELs & ENDPOINTS FOR DEVELOPMENTAL TOXICITY STUDIES IN RATS						
CHEMICAL	MATERNAL TOXICITY			DEVELOPMENTAL TOXICITY		
	(mg/kg/day)		ENDPOINT	(mg/kg/day)		ENDPOINT
	NOEL	LOEL		NOEL	LOEL	
14) ETHION	0.6	2.5	Hyperactivity	0.6	2.5	Delayed ossification of pubes in the fetuses.
15) ETHOPROP	2.0	9.0	Decreases in body weight gain and increased incidence of soft stools.	≥18.0	NA	No developmental toxicity at HDT.
16) ETHYL PARATHION	1.0	1.5	Increased mortality and decreased body weights.	1.5	NA	No developmental toxicity at HDT.
17) FENAMIPHOS	0.85	3.0	Increased mortality and decreases in body weight gain and food consumption.	≥3.0	NA	No developmental toxicity at HDT.
18) FENTHION	4.2 <1.0 (ChoI)	18.0	Clinical signs (hypoactivity, urine stains) and decreased body weight gain. Plasma, RBC and Brain ChEI.	4.2	18.0	Increase in post implantation loss and increase in fetal Brain ChEI.
19) FENITROTHION	8.0	25.0	Clinical signs (tremors) and decreased body weight and body weight gains.	8.0	25.0	Increased incidence (fetal and litter) fetuses with one full and one rudimentary 13th ribs.
20) FONOFOS	NO DATA AVAILABLE					
21) ISOFENPHOS	0.05	0.45	Plasma, RBC & Brain ChEI.	≥4.0	NA	No developmental toxicity at HDT.
22) ISAZOPHOS	NO DATA AVAILABLE					
23) MALATHION	400.0	800.0	Clinical signs (urine stain) and decreases in body weight and food consumption.	≥800.0	NA	No developmental toxicity at HDT.
24) METHIDATHION	1.0	2.25	Increased mortality, cholinergic signs, and decreases in body weight gain and food consumption.	≥2.25	NA	No developmental toxicity at HDT.

ATTACHMENT 1. NOELs/LOELs & ENDPOINTS FOR DEVELOPMENTAL TOXICITY STUDIES IN RATS						
CHEMICAL	MATERNAL TOXICITY			DEVELOPMENTAL TOXICITY		
	(mg/kg/day)		ENDPOINT	(mg/kg/day)		ENDPOINT
	NOEL	LOEL		NOEL	LOEL	
25) METHAMIDOPHOS	1.0	3.0	Cholinergic signs and decreases in body weight gain and food consumption.	1.0	3.0	Decreased fetal body weight.
26) METHYL PARATHION	1.0	3.0	Increased mortality, cholinergic signs, plasma, erythrocyte and brain ChEI, decreases in body weight, body weight gain and food consumption.	1.0	3.0	Increased postimplantation loss (early resorptions), decreased fetal body weight, increased incidence of delayed ossification (3rd cervical vertebrae, proximal phalanx of the 2nd right digit, and 1st metatarsal of both hind limbs).
27) NALED	10.0	40.0	Cholinergic signs.	≥40.0	NA	No developmental toxicity at HDT.
28) OXYDEMETON-METHYL	NA	0.5	Plasma & Brain ChEI at LDT.	≥4.5	NA	No developmental toxicity at HDT.
29) PHORATE	0.25	0.5	Increased mortality and clinical signs (convulsions and hypothermia).	0.25	0.5	No developmental toxicity at HDT.
	0.3	0.4	Mortality, neurotoxic clinical signs, decreases in body weight, body weight gain, and food consumption and gross pathology.	0.3	0.4	Decreased fetal body weights and increased incidence of skeletal variations (delayed ossification of the sternum and pelvis).
30) PHOSMET	10	15	Decreased body weight gain and food consumption and clinical signs.	≥15	NA	No developmental toxicity at HDT.
31) PHOSTEBUPIRIM	0.5	0.75	Increased mortality, cholinergic signs, plasma, RBC and brain ChEI, and decreased body weight and food consumption.	≥0.75	NA	No developmental toxicity at HDT.
32) PIRIMIPHOS METHYL	15.0	150.0	Clinical signs (tremors, abnormal gait, irregular respiration, urinary incontinence)	≥150.0	NA	No developmental toxicity at HDT.

ATTACHMENT 1. NOELs/LOELs & ENDPOINTS FOR DEVELOPMENTAL TOXICITY STUDIES IN RATS						
CHEMICAL	MATERNAL TOXICITY			DEVELOPMENTAL TOXICITY		
	(mg/kg/day)		ENDPOINT	(mg/kg/day)		ENDPOINT
	NOEL	LOEL		NOEL	LOEL	
33) PROFENOFOS	30.0	60.0	Decreases in body wight gain and food consumption.	≥60.0	NA	No developmental toxicity at HDT.
34) PROPETAMPHOS	1.5	3.0	Cholinergic signs.	≥6.0	NA	No developmental toxicity at HDT.
35) SULFOTEPP	INADEQUATE DATA BASE					
36) TEMEPHOS	≥30.0	NA	No maternal toxicity at HDT. Study inadequate since high dose did not elicit any toxicity in the dams.	≥30.0	NA	No developmental toxicity at HDT. Study classified inadequate due to lack of maternal toxicity at HDT.
37) TERBUFOS	≥0.2	NA	No maternal toxicity at HDT	0.1	0.2	Increases in early fetal resorptions, number of litters with two or more resorptions, and postimplantation losses.
38)TETRACHLORVINPHOS	75.0	150.0	Decreased body weight gain.	≥300.0	NA	No developmental toxicity at HDT.
39) TRIBUFOS (DEF)	1.0	7.0	Plasma and RBC ChEI.	≥28.0	NA	No developmental toxicity at HDT.
40) TRICHLORFON	NA	≥45	Plasma and Brain ChEI.	NA	≥45.0	Increases in delayed ossification of skulls, vertebrae and sternebrae in fetuses. Study supplementary - technical deficiencies)

ATTACHMENT 2

NOELs/LOELs and ENDPOINTS FOR DEVELOPMENTAL TOXICITY STUDIES IN RABBITS

ATTACHMENT 2. NOELs/LOELs & ENDPOINTS FOR DEVELOPMENTAL TOXICITY STUDIES IN RABBITS						
CHEMICAL	MATERNAL TOXICITY			DEVELOPMENTAL TOXICITY		
	(mg/kg/day)		ENDPOINT	(mg/kg/day)		ENDPOINT
	NOEL	LOEL		NOEL	LOEL	
1) ACEPHATE	3.0	10.0	Abortions and increased nasal discharge.	≥10.0	NA	No developmental toxicity at HDT.
2) AZINPHOS METHYL	1.0	2.5	Plasma & RBC ChEI	2.5	6.0	Increases in pre-and postimplantation losses.
3) BENSULIDE	20.0	80.0	Decreased body weight and body weight gain.	≥80.0	Not Achieved (NA)	No developmental toxicity at HDT.
4) CADUSAFOS	0.3	0.9	Increased mortality and cholinergic signs	0.3	0.9	Increase in total number of resorptions, decrease in total number of fetuses and fetal death.
5) CHLORETHOXYFOS	0.76	1.38	Increased mortality associated with ChEI.	1.38	2.1	Increase in early resorptions/litter along with increase in the number of litters with at least one early resorption/total litter.
6) CHLORPYRIFOS	81.0	140.0	Decrease in body weight.	81.0	140.0	Decreases in fetal weight and length, increased incidence of skeletal variations and ossification delays in the sternebrae
7) CHLORPYRIFOS-METHYL	≥16.0	NA	**STUDY UNACCEPTABLE**	≥16.0	NA	**STUDY UNACCEPTABLE**
8) COUMAPHOS	2.0	18.0	Increased mortality and cholinergic signs.	≥18.0	NA	No developmental toxicity at HDT.
9) DICHLORVOS (DDVP)	0.1	2.5	Increased mortality, cholinergic signs and decreases in body weight and body weigh gain.	≥7	NA	No developmental toxicity at HDT.
10) DIAZINON	25	100	Increased mortality.	≥100	NA	No developmental toxicity at HDT.
11) DICROTOPHOS	--	--	**STUDY UNACCEPTABLE**	--	--	**STUDY UNACCEPTABLE**
12) DIMETHOATE	10.0	20.0	Decreased body weight gain	20.0	40.0	Decreased fetal body weight.

ATTACHMENT 2. NOELs/LOELs & ENDPOINTS FOR DEVELOPMENTAL TOXICITY STUDIES IN RABBITS						
CHEMICAL	MATERNAL TOXICITY			DEVELOPMENTAL TOXICITY		
	(mg/kg/day)		ENDPOINT	(mg/kg/day)		ENDPOINT
	NOEL	LOEL		NOEL	LOEL	
13) DISULFOTON	1.0	1.5	Cholinergic signs (tremors, unsteadiness/ incoordination and increased respiration)	≥5	NA	No developmental toxicity at HDT.
14) ETHION	2.4	9.6	Clinical signs (orange color urine) and decreases in body weight gain and food consumption.	≥9.6	NA	No developmental toxicity at HDT.
15) ETHOPROP	≥2.5	NA	No maternal toxicity at HDT.	≥2.5	NA	No developmental toxicity at HDT.
16) ETHYL PARATHION	4.0	16.0	Mortality, increased moribundity and decreases in body weight and body weight gain.	4.0	16.0	Decreased litter size.
17) FENAMIPHOS	0.5	2.5	Cholinergic signs.	≥2.5	NA	No developmental toxicity at HDT.
18) FENTHION	1.0	2.75	Clinical signs (soft stools).	2.75	7.5	Increased resorptions, decreased fetal weight, decreased metacarpal ossification and decreased incidence of extra ribs in the number of fetuses but not in the number of litters.
19) FENNITROTHION	10.0	30.0	Increased mortality, cholinergic signs and decreased body weight gains.	≥30.0	NA	No developmental toxicity at HDT.
20) FONOFOS	NO DATA AVAILABLE					
21) ISOFENPHOS	0.25 Sys. 1.25	1.25 Sys 7.5	Plasma, RBC & Brain ChEI. Increased mortality and decreases in body weight and body weight gains.	≥7.5	NA	No developmental toxicity at HDT.
22) ISAZOPHOS	NO DATA AVAILABLE					
23) MALATHION	25.0	50.0	Decreased body weight gain.	25.0	50.0	Slight increase in mean resorption sites.

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ATTACHMENT 2. NOELs/LOELs & ENDPOINTS FOR DEVELOPMENTAL TOXICITY STUDIES IN RABBITS						
CHEMICAL	MATERNAL TOXICITY			DEVELOPMENTAL TOXICITY		
	(mg/kg/day)		ENDPOINT	(mg/kg/day)		ENDPOINT
	NOEL	LOEL		NOEL	LOEL	
24) METHIDATHION	6.0	12.0	Cholinergic signs	≥12.0	NA	No developmental toxicity at HDT.
25)METHIDAMIDOPHOS	0.2	0.65	Decreased body weight gain and food consumption.	≥2.5	NA	No developmental toxicity at HDT.
26) METHYL PARATHION	≥3.0	NA	No maternal toxicity at HDT.	≥3.0	NA	No developmental toxicity at HDT.
27) NALED	≥8.0	NA	No maternal toxicity at HDT.	≥8.0	NA	No developmental toxicity at HDT.
28) OXYDEMETON- METHYL	0.2	0.8	Erythrocyte & Brain ChEI.	≥0.8	NA	No developmental toxicity at HDT.
29) PHORATE	0.15	0.5	Increased mortality and body weight loss.	≥1.2	NA	No developmental toxicity at HDT.
30) PHOSMET	5	15	Clinical signs and decreased body weight.	5	15	Increased incidence of skeletal variations in fetuses.
31) PHOSTEBUPIRIM	0.1	0.3	Erythrocyte ChEI.	≥0.3	NA	No developmental toxicity at HDT.
32) PIRIMIPHOS METHYL	12.0	24.0	Plasma & RBC ChEI.	≥48.0	NA	No developmental toxicity at HDT.
33) PROFENOFOS	30.0	60.0	Decreased body weight gain.	≥60.0	NA	No developmental toxicity at HDT.
34) PROPETAMPHOS	4	8	Decreased body weight gain	4	8	Increased resorption.
35) SULFOTEPP	INADEQUATE DATA BASE					
36) TEMEPHOS	NO DATA/ NO STUDY					
37) TERBUFOS	0.1	0.25	Clinical signs (soft stools) and decreased body weight gain.	0.25	0.5	Increased resorptions and decreased fetal body weights.

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ATTACHMENT 2. NOELs/LOELs & ENDPOINTS FOR DEVELOPMENTAL TOXICITY STUDIES IN RABBITS						
CHEMICAL	MATERNAL TOXICITY			DEVELOPMENTAL TOXICITY		
	(mg/kg/day)		ENDPOINT	(mg/kg/day)		ENDPOINT
	NOEL	LOEL		NOEL	LOEL	
38)TETRACHLORVINPHOS	375.0	750.0	Increased mortality and abortions and clinical signs (red vaginal fluid).	375.0	750.0	Increase in early resorptions/dam with a corresponding increase in postimplantation loss and a decrease in live fetuses/dam.
39) TRIBUFOS (DEF)	NA Sys. 3.0	1.0 Sys. 9.0	Plasma & RBC ChEI Decreased body weight gain.	≥9.0	NA	No developmental toxicity at HDT.
40) TRICHLORFON	10.0	35.0	Abortions and RBC and Brain ChEI.	35.0	110.0	Increase in number of does with resorptions, decreased male fetal body weight and delayed ossification.

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ATTACHMENT 3

NOELs/LOELs and ENDPOINTS FOR THE TWO-GENERATION REPRODUCTION STUDIES IN RATS

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ATTACHMENT 3. NOELs/LOELs & ENDPOINTS FOR THE 2-GENERATION REPRODUCTION TOXICITY STUDIES IN RATS						
CHEMICAL	PARENTAL SYSTEMIC TOXICITY (mg/kg/day) NOEL	PARENTAL SYSTEMIC TOXICITY (mg/kg/day) LOEL	PARENTAL SYSTEMIC TOXICITY ENDPOINT	OFF SPRING TOXICITY (mg/kg/day) NOEL	OFF SPRING TOXICITY (mg/kg/day) LOEL	OFF SPRING TOXICITY ENDPOINT
1) ACEPHATE	2.5	25	Decreased body weight gain and clinical signs (alopecia and soft stool).	2.5	25	Decreased viability index and decreased pup body weight gain.
2) AZINPHOS METHYL	0.75	2.25	Increased mortality, decreased body weight and clinical signs (poor coordination and convulsions).	0.25	0.75	Decrease in pup viability and lactation indices
	Not Achieved (NA)	0.55	Plasma& RBC ChEI. 1-Generation Study	0.55	1.54	Decrease in pup viability index and decreased pup body weights on post natal days (PD) 14 and 21.
3) BENSULIDE	2.6	15.4	RBC ChEI in F1	15.4	93.2	Decreased F2 pup survival.
4) CADUSAFOS	0.025	0.25	Plasma & RBC ChEI.	≥0.25	NA	No offspring toxicity at HDT.
5) CHLORETHOXYFOS	0.296	0.607	Tremors during lactation.	0.607	NA	No offspring toxicity at HDT.
6) CHLORPYRIFOS	0.1	0.3	Plasma & RBC ChEI.	≥1.0	NA	No offspring toxicity at HDT.
	0.8	1.2	Decrease in body weight gains in males	≥1.2	NA	No offspring toxicity at HDT.
	≥3.58	NA	No parental systemic toxicity at HDT.	≥ 3.58	NA	No offspring toxicity at HDT.
	0.1	1.0	Plasma & RBC ChEI and adrenal gland lesions.	1.0	5.0	Increased postnatal mortality and reduced pup body weight.
7) CHLORPYRIFOS-METHYL	--	--	STUDY UNACCEPTABLE	--	--	STUDY UNACCEPTABLE
8) COUMAPHOS	≥1.79	NA	No parental systemic toxicity at HDT.	≥1.79	NA	No offspring toxicity at HDT.
9) DICHLORVOS (DDVP)	2.3	8.3	Decreased % of females with estrous cycle and increased % of females cycling with abnormal cycle.	2.3	8.3	Reduced dams bearing litters, fertility index, pregnancy index, pup weight.

ATTACHMENT 3. NOELs/LOELs & ENDPOINTS FOR THE 2-GENERATION REPRODUCTION TOXICITY STUDIES IN RATS						
CHEMICAL	PARENTAL SYSTEMIC TOXICITY (mg/kg/day)		ENDPOINT	OFF SPRING TOXICITY (mg/kg/day)		ENDPOINT
	NOEL	LOEL		NOEL	LOEL	
10) DIAZINON	0.67	6.69	Decreased body weight gain.	0.67	6.69	Pup mortality, decreased pup weight gained during lactation.
11) DICROTOPHOS	0.025	0.25	Decreases in body weight and food utilization.	0.025	0.25	Reduced no. Of F2 pups/liter during lactation.
12) DIMETHOATE	0.08	1.2	ChEI in both sexes in all generations.	1.2	5.46	Decreases in number of live pups, pup body weights, and fertility in F1a, F1b, F2a and F2b matings.
13) DISULFOTON	0.025	0.1	Plasma and RBC ChEI.	0.1	0.45	Pup mortality and pup weight decrements
14) ETHION	0.2	1.25	Plasma ChEI	≥1.25	NA	No offspring toxicity at HDT.
15) ETHOPROP	2.3	13.0	Decrease in body weight gain.	2.3	13.0	Increased pup mortality PD 21& 28 and decreased pup body weight gain in both generations
16) ETHYL PARATHION	0.05	0.5	Plasma, RBC & Brain ChEI.	≥1.0	NA	No offspring toxicity at HDT.
17) FENAMIPHOS	0.17	0.64	Plasma & RBC ChEI.	≥3.2	NA	No offspring toxicity at HDT.
18) FENTHION	0.1	0.7	Epididymal vacuolation and Plasma & RBC ChEI.	0.1	0.7	Plasma ChEI.
19) FENITROTHION	2.74	8.4	Decreases in body weight, body weight gains and food consumption.	2.74	8.4	Decreases in fertility, number of implantation sites, viability and lactation in one generation.
20) FONOFOS	NO DATA AVAILABLE					
21) ISOFENPHOS	0.08	0.44	Plasma, RBC and/or Brain ChEI.	0.08	0.44	Increased pup mortality (reductions in lactation indices and mean litter sizes) and clinical signs (small to very small emaciated pups).
22) ISAZOPHOS	NO DATA AVAILABLE					

ATTACHMENT 3.	NOELs/LOELs & ENDPOINTS FOR THE 2-GENERATION REPRODUCTION TOXICITY STUDIES IN RATS					
	PARENTAL SYSTEMIC TOXICITY			OFF SPRING TOXICITY (mg/kg/day)		
	(mg/kg/day)			(mg/kg/day)		
CHEMICAL	NOEL	LOEL	ENDPOINT	NOEL	LOEL	ENDPOINT
23) MALATHION	394.0	612	Decreased body weights of F1 during gestation and lactation and decreased F1 pre-mating body weight.	131.0	394.0	Decreased F1a and F2b pup body weight during lactation Day 21.
24) METHIDATHION	0.25	1.25	Tremors, decreased food consumption during lactation and decreased ovarian weights.	0.25	1.25	Decreased pup body weight and clinical signs (hypothermia and appearance of starvation).
25) METHAMIDOPHOS	0.5	1.65	Decreased body weight.	0.5	1.65	Decreased pup viability and body weight during lactation Day 14.
26) METHYL PARATHION	0.44	2.3	Decreased premating body weight for F1 females and decreased maternal body weight during lactation for both generations.	0.44	2.3	Decreased pup survival in early lactation and decreased body weight gain and increased food consumption immediately after weaning.
27) NALED	6.0	18.0	Decreased body weight gains.	≥18.0	NA	No offspring toxicity at HDT.
28) OXYDEMETON-METHYL	0.05	0.5	Decreased body weight for both sexes for entire study and for females during gestation.	0.05	0.5	Decreased viability index and pup body weight during lactation at Day 5 .
	0.38	2.1	Decreases in male and female fertility of unknown origin in P and F1 generations.	0.38	2.1	Decreased litter size at birth and decreased pup weight during lactation.
29) PHORATE	0.2	0.4	Tremors and Plasma and Brain ChEI	0.2	0.4	Decrease in pup survival during early lactation and decrease in pup weight during late lactation.
30) PHOSMET	≤1.5	6.1	RBC ChEI.	1.5	6.1	Decreased number of live pup/litter, pup weights, fertility index and lactation index.
31) PHOSTEBUPIRIM	0.05	0.25	Plasma & RBC ChEI.	0.25	1.25	Tremors in neonates, decreased pup body weight gain, increase in pup mortality, and ChEI on PD 21 but not on PD 4.
32) PIRIMIPHOS-METHYL	NA	0.87	Plasma ChEI at LDT.	≥13.72	NA	No offspring toxicity at HDT.

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ATTACHMENT 3. NOELs/LOELs & ENDPOINTS FOR THE 2-GENERATION REPRODUCTION TOXICITY STUDIES IN RATS						
	PARENTAL SYSTEMIC TOXICITY			OFF SPRING TOXICITY (mg/kg/day)		
	(mg/kg/day)			(mg/kg/day)		
CHEMICAL	NOEL	LOEL	ENDPOINT	NOEL	LOEL	ENDPOINT
33) PROFENOFOS	7.3	29.0	Decreased body weight gain and food consumption.	7.3	29.0	Decreased pup body weight in both sexes of F1 and F2 and cumulative body weight gain on PD 14 and 21.
34) PROPETAMPHOS	0.3	2.1	RBC & Brain ChEI.	0.3	2.1	Plasma & RBC ChEI.
35) SULFOTEPP	NO DATA AVAILABLE					
36) TEMEPHOS	≥6.25	NA	No parental systemic toxicity at HDT. Study unacceptable since the high dose did not elicit any systemic toxicity in the parental animals.	≥6.25	NA	No toxicity to the offspring at HDT. However, doses for parental animals are inadequate since there were no systemic toxicity to the parental animals.
37) TERBUFOS	0.08	0.22	Decreased body weight gain during lactation.	0.07	0.17	Decrease in pregnancy rate and male fertility.
38) TETRACHLORVINPHOS	25.0	100.0	Decreased body weight gain in males in Fo and in both sexes in F1 and increased mean adrenal gland weights in Fo females.	≥100.0	NA	No offspring toxicity at HDT.
39) TRIBUFOS (DEF)	NA	0.2	Plasma ChEI.	1.7	15.0	Increases in number of litters with still born pups and pup death throughout lactation, decreases in F1 and F2 pup body weights and increases in F1 gestation period.
40) TRICHLORFON	NA	15.0	Plasma and Brain ChEI in both generations.	50.0	175.0	Decreases in F1 pup body weights on PD 7 and 21 and presence of dilated renal pelvis.
	15.0	50.0	Decreased body weight gain.	15.0	50.0	Based on reduced fertility during F0 matings (lower litter size).

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ATTACHMENT 4

SUMMARY OF HAZARD IDENTIFICATION ASSESSMENT REVIEW COMMITTEE FQPA ASSESSMENT

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ATTACHMENT 4. SUMMARY OF HAZARD IDENTIFICATION ASSESSMENT REVIEW COMMITTEE FQPA ASSESSMENT							
PESTICIDE	ACUTE DELAYED NEUROTOXICITY HEN	MAMMALIAN NEUROTOXICITY - RAT		EVIDENCE OF ENHANCED SUSCEPTIBILITY IN DEVELOPMENTAL STUDIES RAT & RABBIT	EVIDENCE OF ENHANCED SUSCEPTIBILITY IN THE 2-GENERATION REPRODUCTION RAT	REQUIREMENT OF A DEVELOPMENTAL NEUROTOXICITY STUDY IN RATS	DATA GAPS
		ACUTE	SUBCHRONIC				
1) ACEPHATE	OPIDN: Negative Neuropathology: Negative NTE: Negative Literature Data NTE: Positive	Neuropathology: Negative Cholinesterase activity measured (ChEI):Yes	Neuropathology: Negative ChEI measured: Yes	No increased Susceptibility	No increased Susceptibility	Not Required	None
2) AZINPHOS-METHYL	OPIDN: Negative Neuropathology: Negative Confirmatory NTE Study Required	Neuropathology: Negative ChEI measured: Yes	Neuropathology: Negative ChEI measured: Yes	No increased Susceptibility	No increased Susceptibility	Not Required	None
3) BENSULIDE	OPIDN: Negative NTE: Negative	Neuropathology: Negative ChEI measured: Yes	Study Waived	No increased Susceptibility	No increased Susceptibility	Not Required	None

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ATTACHMENT 4. SUMMARY OF HAZARD IDENTIFICATION ASSESSMENT REVIEW COMMITTEE FQPA ASSESSMENT							
PESTICIDE	**ACUTE DELAYED NEUROTOXICITY HEN**	**MAMMALIAN NEUROTOXICITY - RAT**		**EVIDENCE OF ENHANCED SUSCEPTIBILITY IN DEVELOPMENTAL STUDIES RAT & RABBIT**	**EVIDENCE OF ENHANCED SUSCEPTIBILITY IN THE 2-GENERATION REPRODUCTION RAT**	**REQUIREMENT OF A DEVELOPMENTAL NEUROTOXICITY STUDY IN RATS**	**DATA GAPS**
		ACUTE	**SUBCHRONIC**				
4) CADUSAFOS	Inadequate Study (No histopathology or NTE data) Confirmatory NTE Study Required	Not available	Not available	No increased Susceptibility	No increased Susceptibility	**Reserved** Pending Acute Hen, Acute & 90-day rat neurotoxicity studies	Acute-Hen Acute -Rat Neurotoxicity 90-Day -Rat Neurotoxicity
		No data to assess neurotoxicity, cholinesterase inhibition, behavioral effects, or neuropathology					
5) CHLORETHOXYFOS	OPIDN: Negative Neuropathology: Negative	Neuropathology: Negative ChEI measured: Yes	Waived since other studies showed no evidence of neuropathology	No increased Susceptibility	No increased Susceptibility	Not Required	None
6) CHLORPYRIFOS	OPIDN: Negative <u>Literature Data</u> OPIDN: Positive NTE: Positive	Neuropathology: Negative ChEI measured: Yes	Neuropathology: Negative ChEI measured: Yes	No increased Susceptibility <u>Literature Data</u> Enhanced susceptibility seen in young rats (ChEI, behavioral and other developmental neurotoxic effects).	No increased Susceptibility	**Required** Literature Data OPIDN: Positive	Developmental Neurotoxicity Study in Rats

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ATTACHMENT 4. SUMMARY OF HAZARD IDENTIFICATION ASSESSMENT REVIEW COMMITTEE FQPA ASSESSMENT							
PESTICIDE	**ACUTE DELAYED NEUROTOXICITY HEN**	**MAMMALIAN NEUROTOXICITY - RAT**		**EVIDENCE OF ENHANCED SUSCEPTIBILITY IN DEVELOPMENTAL STUDIES RAT & RABBIT**	**EVIDENCE OF ENHANCED SUSCEPTIBILITY IN THE 2-GENERATION REPRODUCTION RAT**	**REQUIREMENT OF A DEVELOPMENTAL NEUROTOXICITY STUDY IN RATS**	**DATA GAPS**
		ACUTE	**SUBCHRONIC**				
7) CHLORPYRIFOS - METHYL	Equivocal evidence of neuropathology	Not available	Not available	Studies Unacceptable To Assess Susceptibility	Study Unacceptable To Assess Susceptibility	Can Not Be Ascertained Due to Inadequate Data Base	Acute Rat 90-Day Rat Neurotoxicity Developmental -Rat & Rabbit 2-Generation Reproduction
		No data to assess neurotoxicity, cholinesterase inhibition, behavioral effects, or neuropathology					
8) COUMAPHOS	OPIDN: Negative Neuropathology: Negative Confirmatory NTE Study Required	Not available	Not available	No increased Susceptibility	No increased Susceptibility	**Reserved**. Pending Acute & 90-day neurotoxicity studies	Acute - Rat 90-Day-Rat

ATTACHMENT 4. SUMMARY OF HAZARD IDENTIFICATION ASSESSMENT REVIEW COMMITTEE FQPA ASSESSMENT							
PESTICIDE	**ACUTE DELAYED NEUROTOXICITY HEN**	**MAMMALIAN NEUROTOXICITY - RAT**		**EVIDENCE OF ENHANCED SUSCEPTIBILITY IN DEVELOPMENTAL STUDIES RAT & RABBIT**	**EVIDENCE OF ENHANCED SUSCEPTIBILITY IN THE 2-GENERATION REPRODUCTION RAT**	**REQUIREMENT OF A DEVELOPMENTAL NEUROTOXICITY STUDY IN RATS**	**DATA GAPS**
		ACUTE	**SUBCHRONIC**				
9) DICHLROVOS (DDVP)	Acute OPIDN: Equivocal 28-day Neuropathology: Negative NTE: Negative	Neuropathology Negative ChEI measured: Yes	Neuropathology Negative ChEI measured: Yes	No increased Susceptibility	No increased Susceptibility	**Reserved** Pending results of developmental toxicity study in Guinea Pigs requested by HIARC. See HIARC Report.	None
10) DIAZINON	OPIDN: Negative Neuropathology: Negative NTE: Negative	Neuropathology Negative ChEI measured: Yes	Neuropathology Negative ChEI measured: Yes	No increased Susceptibility	No increased Susceptibility	Not Required	None
11) DICROTOPHOS	Unacceptable study	Neuropathology: Negative	Neuropathology Negative	FQPA ASSESSMENT COULD NOT BE MADE DUE TO INADEQUATE DATA BASE			

ATTACHMENT 4. SUMMARY OF HAZARD IDENTIFICATION ASSESSMENT REVIEW COMMITTEE FQPA ASSESSMENT							
PESTICIDE	ACUTE DELAYED NEUROTOXICITY HEN	MAMMALIAN NEUROTOXICITY - RAT		EVIDENCE OF ENHANCED SUSCEPTIBILITY IN DEVELOPMENTAL STUDIES RAT & RABBIT	EVIDENCE OF ENHANCED SUSCEPTIBILITY IN THE 2-GENERATION REPRODUCTION RAT	REQUIREMENT OF A DEVELOPMENTAL NEUROTOXICITY STUDY IN RATS	DATA GAPS
		ACUTE	SUBCHRONIC				
12) DIMETHOATE	OPIDN: Negative Neuropathology: Negative NTE: Equivocal Confirmatory NTE study Required	Neuropathology: Negative ChEI measured: No.	Neuropathology: Negative ChEI measured: Yes	No increased Susceptibility	No increased Susceptibility	Not Required	None
13) DISULFOTON	Unacceptable Study	Neuropathology: Negative ChEI measured: Yes	Neuropathology: Equivocal ChEI measured: Yes	No increased Susceptibility	No increased Susceptibility	**Reserved** Pending Acute Hen study	Acute Hen
14) ETHION	OPIDN: Negative Neuropathology: Negative Confirmatory NTE Study Required	Neuropathology: Negative ChEI measured: No	Equivocal neuropathology at high dose ChEI measured: No	No increased Susceptibility	No increased Susceptibility	Not required	None

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ATTACHMENT 4. SUMMARY OF HAZARD IDENTIFICATION ASSESSMENT REVIEW COMMITTEE FQPA ASSESSMENT							
PESTICIDE	ACUTE DELAYED NEUROTOXICITY HEN	MAMMALIAN NEUROTOXICITY - RAT		EVIDENCE OF ENHANCED SUSCEPTIBILITY IN DEVELOPMENTAL STUDIES RAT & RABBIT	EVIDENCE OF ENHANCED SUSCEPTIBILITY IN THE 2-GENERATION REPRODUCTION RAT	REQUIREMENT OF A DEVELOPMENTAL NEUROTOXICITY STUDY IN RATS	DATA GAPS
		ACUTE	SUBCHRONIC				
15) ETHOPROP	OPIDN: Negative Neuropathology: Negative NTE requested by RfD Committee 5/96	Neuropathology: Negative ChEI measured: Yes	Neuropathology: Negative ChEI measured: Yes	No increased Susceptibility	No increased Susceptibility	Not Required	None
16) ETHYL PARATHION	OPIDN: Negative NTE : Negative Neuropathology: Negative	Neuropathology: Negative ChEI measured: Yes	Neuropathology: Negative ChEI measured: Yes	No increasd Susceptibility	No increased Susceptibility	Not Required	None
17) FENAMIPHOS	OPIDN: Negative Neuropathology: Negative Confirmatory NTE Study Required	Neuropathology: Negative ChEI measured: Yes	Neuropathology: Negative ChEI measured: Yes	No increased Susceptibility	No increased Susceptibility	Not required	None
18) FENITROTHION	OPIDN: Negative Neuropathology: Negative Confirmatory NTE Study Required	Neuropathology: Negative ChEI measured: No	Neuropathology: Negative ChEI measured: Yes	No increased Susceptibility	No increased Susceptibility	Not required	None

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ATTACHMENT 4. SUMMARY OF HAZARD IDENTIFICATION ASSESSMENT REVIEW COMMITTEE FQPA ASSESSMENT							
PESTICIDE	**ACUTE DELAYED NEUROTOXICITY HEN**	**MAMMALIAN NEUROTOXICITY - RAT**		**EVIDENCE OF ENHANCED SUSCEPTIBILITY IN DEVELOPMENTAL STUDIES RAT & RABBIT**	**EVIDENCE OF ENHANCED SUSCEPTIBILITY IN THE 2-GENERATION REPRODUCTION RAT**	**REQUIREMENT OF A DEVELOPMENTAL NEUROTOXICITY STUDY IN RATS**	**DATA GAPS**
		ACUTE	**SUBCHRONIC**				
19) FENTHION	Acute (Oral & Dermal) OPIDN: Negative Neuropathology: Negative NTE: Negative Subchronic OPIDN: Negative Neuropathology: Negative	Neuropathology: Negative ChEI measured: Yes	Neuropathology: Negative ChEI measured: Yes	No increased Susceptibility	No increased Susceptibility	No Required	None
20) FONOFOS	NO DATA AVAILABLE						

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ATTACHMENT 4. SUMMARY OF HAZARD IDENTIFICATION ASSESSMENT REVIEW COMMITTEE FQPA ASSESSMENT							
PESTICIDE	ACUTE DELAYED NEUROTOXICITY HEN	MAMMALIAN NEUROTOXICITY - RAT		EVIDENCE OF ENHANCED SUSCEPTIBILITY IN DEVELOPMENTAL STUDIES RAT & RABBIT	EVIDENCE OF ENHANCED SUSCEPTIBILITY IN THE 2-GENERATION REPRODUCTION RAT	REQUIREMENT OF A DEVELOPMENTAL NEUROTOXICITY STUDY IN RATS	DATA GAPS
		ACUTE	SUBCHRONIC				
21) ISOFENPHOS	Acute OPIDN: Negative Neuropathology: Negative Confirmatory NTE Study Required Subchronic OPIDN: Negative Neuropathology: Negative	Neuropathology: Negative ChEI measured: Yes	Neuropathology: Negative ChEI measured: Yes	No increased Susceptibility	No increased Susceptibility	Not Required	None
22) ISAZOPHOS	NO DATA AVAILABLE						
23) MALATHION	OPIDN: Negative Neuropathology: Negative **Literature Data** NTE:-Negative	Neuropathology: Negative ChEI measured: Yes	Neuropathology: Negative ChEI measured: Yes	No increased Susceptibility	No increased Susceptibility	Not required	None

ATTACHMENT 4. SUMMARY OF HAZARD IDENTIFICATION ASSESSMENT REVIEW COMMITTEE FQPA ASSESSMENT							
PESTICIDE	ACUTE DELAYED NEUROTOXICITY HEN	MAMMALIAN NEUROTOXICITY - RAT		EVIDENCE OF ENHANCED SUSCEPTIBILITY IN DEVELOPMENTAL STUDIES RAT & RABBIT	EVIDENCE OF ENHANCED SUSCEPTIBILITY IN THE 2-GENERATION REPRODUCTION RAT	REQUIREMENT OF A DEVELOPMENTAL NEUROTOXICITY STUDY IN RATS	DATA GAPS
		ACUTE	SUBCHRONIC				
24) METHAMIDOPHOS	Acute & Subchronic OPIDN: Negative Neuropathology: Negative NTE: Negative (Acute) Positive (subchronic) *Racemate & Enantiomers* **Positive** for OPIDN at extremely high levels **Literature Data** Polyneuropathy & peripheral neuropathy in humans at high doses. Polyneuropathy in adult hens at high doses	Neuropathology: Negative ChEI measured: Yes	Neuropathology: Negative ChEI measured: Yes	No increased Susceptibility	No increased Susceptibility	**Required** Positive NTE Polyneuropathy in hens and Delayed peripheral neuropathy in humans in published studies	Developmental Neurotoxicity Study in Rats

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ATTACHMENT 4. SUMMARY OF HAZARD IDENTIFICATION ASSESSMENT REVIEW COMMITTEE FQPA ASSESSMENT							
PESTICIDE	**ACUTE DELAYED NEUROTOXICITY HEN**	**MAMMALIAN NEUROTOXICITY - RAT**		**EVIDENCE OF ENHANCED SUSCEPTIBILITY IN DEVELOPMENTAL STUDIES RAT & RABBIT**	**EVIDENCE OF ENHANCED SUSCEPTIBILITY IN THE 2-GENERATION REPRODUCTION RAT**	**REQUIREMENT OF A DEVELOPMENTAL NEUROTOXICITY STUDY IN RATS**	**DATA GAPS**
		ACUTE	**SUBCHRONIC**				
25) METHIDATHION	OPIDN: Negative Neuropathology: Negative Confirmatory NTE Study Required	Neuropathology: Negative ChEI measured: Yes	Negative for neuropathology ChEI measured: Yes	No increased Susceptibility	No increased Susceptibility	Not required	None
26) METHYL PARATHION	OPIDN: Negative Neuropathology: Negative Confirmatory NTE Study Required	**Positive** for neuropathology ChEI measured: Yes	**Equivocal** for neuropathology ChEI measured: Yes	No increased Susceptibility in Subdivision F studies. **Literature Data** **Qualitative evidence of increased Susceptibility seen in open literature rat studies via subcutaneous. & intraperitoneal routes at high doses.**	No increased Susceptibility	**Required** Positive neuropathology in acute rat Equivocal neuropathology in subchronic rat Positive Neuropathology in Chronic Rat and 1-Year Rat	Developmental Neurotoxicity Study in Rats

ATTACHMENT 4. SUMMARY OF HAZARD IDENTIFICATION ASSESSMENT REVIEW COMMITTEE FQPA ASSESSMENT							
PESTICIDE	ACUTE DELAYED NEUROTOXICITY HEN	MAMMALIAN NEUROTOXICITY - RAT		EVIDENCE OF ENHANCED SUSCEPTIBILITY IN DEVELOPMENTAL STUDIES RAT & RABBIT	EVIDENCE OF ENHANCED SUSCEPTIBILITY IN THE 2-GENERATION REPRODUCTION RAT	REQUIREMENT OF A DEVELOPMENTAL NEUROTOXICITY STUDY IN RATS	DATA GAPS
		ACUTE	SUBCHRONIC				
27) NALED	Acute OPIDN: Positive Neuropathology: Positive NTE: Negative Subchronic OPIDN: Negative	Neuropathology: Negative ChEI measured: No	Neuropathology: Negative ChEI measured: No	No increased Susceptibility	No increased Susceptibility	Not Required	None
28)OXYDEMETON-METHYL	Acute Neuropathology: Positive Confirmatory NTE Study Required Subchronic Neuropathology: Negative	Neuropathology: Negative ChEI measured: Yes	Neuropathology: Negative ChEI measured: Yes	No increased Susceptibility	No increased Susceptibility	Not Required	Mouse Specific Locus Test.

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ATTACHMENT 4. SUMMARY OF HAZARD IDENTIFICATION ASSESSMENT REVIEW COMMITTEE FQPA ASSESSMENT							
PESTICIDE	ACUTE DELAYED NEUROTOXICITY HEN	MAMMALIAN NEUROTOXICITY - RAT		EVIDENCE OF ENHANCED SUSCEPTIBILITY IN DEVELOPMENTAL STUDIES RAT & RABBIT	EVIDENCE OF ENHANCED SUSCEPTIBILITY IN THE 2-GENERATION REPRODUCTION RAT	REQUIREMENT OF A DEVELOPMENTAL NEUROTOXICITY STUDY IN RATS	DATA GAPS
		ACUTE	SUBCHRONIC				
29) PHORATE	OPIDN: Negative Neuropathology: Negative Confirmatory NTE Study Required.	Not available	Not available	No increased Susceptibility	No increased Susceptibility	**Reserved** Pending Acute & 90-day rat neurotoxicity studies	Acute-Rat Neurotoxicity 90-day Rat Neurotoxicity
		No data to assess neurotoxicity, cholinesterase inhibition, behavioral effects, or neuropathology					
30) PHOSMET	OPIDN: Negative Neuropathology: Negative NTE: Negative Need re-review	Not available	Not available	No increased Susceptibility	No increased Susceptibility	**Reserved** Pending Acute & 90-day rat neurotoxicity studies & Confirmation of results of hen studies	Acute-Rat Neurotoxicity 90-day Rat Neurotoxicity
		No data to assess neurotoxicity, cholinesterase inhibition, behavioral effects, or neuropathology					
31) PHOSTEBUPIRIM	OPIDN: Negative Neuropathology: Negative Confirmatory NTE Study Required	Not available	Not available	No increased Susceptibility	No increased Susceptibility	**Reserved** Pending Acute & 90-day rat neurotoxicity studies	Acute-Rat Neurotoxicity 90-day Rat Neurotoxicity
		No data to assess neurotoxicity, cholinesterase inhibition, behavioral effects, or neuropathology					

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ATTACHMENT 4. SUMMARY OF HAZARD IDENTIFICATION ASSESSMENT REVIEW COMMITTEE FQPA ASSESSMENT							
PESTICIDE	ACUTE DELAYED NEUROTOXICITY HEN	MAMMALIAN NEUROTOXICITY - RAT		EVIDENCE OF ENHANCED SUSCEPTIBILITY IN DEVELOPMENTAL STUDIES RAT & RABBIT	EVIDENCE OF ENHANCED SUSCEPTIBILITY IN THE 2-GENERATION REPRODUCTION RAT	REQUIREMENT OF A DEVELOPMENTAL NEUROTOXICITY STUDY IN RATS	DATA GAPS
		ACUTE	SUBCHRONIC				
32) PIRIMIPHOS-METHYL	No Acute study Subchronic: Unacceptable	Neuropathology: Negative ChEI measured: Yes	Neuropathology: Negative ChEI measured: Yes	No increased Susceptibility	No increased Susceptibility	**Reserved** Pending Acute Hen & Chronic Dog/Rat	Acute-Hen Chronic Toxicity-Dog Chronic Toxicity-Rat
33) PROFENFOS	OPIDN: Negative Neuropathology: Negative Confirmatory NTE Study Required	Neuropathology: Negative ChEI measured: Yes	Neuropathology: Negative ChEI measured: Yes	No increased Susceptibility	No increased Susceptibility	Not Required	None
34) PROPETAMPHOS	OPIDN: Negative Neuropathology: Negative Confirmatory NTE Study Required	Neuropathology: Negative ChEI measured: No	Neuropathology: Negative ChEI measured: No	No increased Susceptibility	No increased Susceptibility	Not Required	None
35) SULFOTEPP	NO DATA AVAILABLE - INADEQUATE DATA BASE						

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ATTACHMENT 4. SUMMARY OF HAZARD IDENTIFICATION ASSESSMENT REVIEW COMMITTEE FQPA ASSESSMENT							
PESTICIDE	**ACUTE DELAYED NEUROTOXICITY HEN**	**MAMMALIAN NEUROTOXICITY - RAT**		**EVIDENCE OF ENHANCED SUSCEPTIBILITY IN DEVELOPMENTAL STUDIES**	**EVIDENCE OF ENHANCED SUSCEPTIBILITY IN THE**	**REQUIREMENT OF A DEVELOPMENTAL NEUROTOXICITY STUDY IN RATS**	**DATA GAPS**
		ACUTE	**SUBCHRONIC**	**RAT & RABBIT**	**2-GENERATION REPRODUCTION RAT**		
36) TEMEPHOS	Study Unacceptable Confirmatory NTE Study Required	Not available	Not available	There are no food uses for this chemical thus requiring only a minimal data base. However, both the oral and dermal developmental toxicity study in rats as well as a three generation reproduction study in rats are unacceptable. Thus, an adequate assessment for FQPA can not be made with the existing database.			
37) TERBUFOS	OPIDN: Negative Neuropathology: Negative Confirmatory NTE Study Required	Not available	Not available	No increased Susceptibility	No increased Susceptibility	**Reserved** Pending Acute & 90-day rat neurotoxicity studies	Acute-Rat Neurotoxicity 90-day Rat Neurotoxicity
		No data to assess neurotoxicity, cholinesterase inhibition, behavioral effects, or neuropathology					
38) TETRACHLOR-VINPHOS	OPIDN: Negative Neuropathology: Negative Confirmatory NTE Study Required	Neuropathology: Negative ChEI measured: No	Neuropathology: Negative ChEI measured: No	No increased Susceptibility	No increased Susceptibility	Not required	None

ATTACHMENT 4. SUMMARY OF HAZARD IDENTIFICATION ASSESSMENT REVIEW COMMITTEE FQPA ASSESSMENT							
PESTICIDE	ACUTE DELAYED NEUROTOXICITY HEN	MAMMALIAN NEUROTOXICITY - RAT		EVIDENCE OF ENHANCED SUSCEPTIBILITY IN DEVELOPMENTAL STUDIES RAT & RABBIT	EVIDENCE OF ENHANCED SUSCEPTIBILITY IN THE 2-GENERATION REPRODUCTION RAT	REQUIREMENT OF A DEVELOPMENTAL NEUROTOXICITY STUDY IN RATS	DATA GAPS
		ACUTE	SUBCHRONIC				
39) TRIBUFOS	Subchronic Dermal OPIDN: Positive Neuropathology: Positive Confirmatory NTE Study Required	Not available	Not available	No increased Susceptibility	No increased Susceptibility	**Required** Evidence of neuropathology in the subchronic hen study	Acute -Hen (subchronic is via the dermal route). Acute - Rat Neurotoxicity 90-day - Rat Neurotoxicity Developmental Neurotoxicity Study in Rats
		No data to assess neurotoxicity, cholinesterase inhibition, behavioral effects, or neuropathology					

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ATTACHMENT 4. SUMMARY OF HAZARD IDENTIFICATION ASSESSMENT REVIEW COMMITTEE FQPA ASSESSMENT							
PESTICIDE	ACUTE DELAYED NEUROTOXICITY HEN	MAMMALIAN NEUROTOXICITY - RAT		EVIDENCE OF ENHANCED SUSCEPTIBILITY IN DEVELOPMENTAL STUDIES RAT & RABBIT	EVIDENCE OF ENHANCED SUSCEPTIBILITY IN THE 2-GENERATION REPRODUCTION RAT	REQUIREMENT OF A DEVELOPMENTAL NEUROTOXICITY STUDY IN RATS	DATA GAPS
		ACUTE	SUBCHRONIC				
40) TRICHLORFON	Acute OPIDN: Positive Neuropathology: Positive Confirmatory NTE Study Required Subchronic OPIDN: Negative Neuropathology: Positive	Not available	In Review	No increased Susceptibility (Rabbit) **Rat (unacceptable)**	No increased Susceptibility	**Reserved** 1)Pending results of the developmental toxicity study in Guinea Pig required by HIARC. 2) Receipt and review of the Developmental toxicity study in rats	Acute-Rat Neurotoxicity 90-day Rat Neurotoxicity Developmental Toxicity Rat
		No data to assess neurotoxicity, cholinesterase inhibition, behavioral effects, or neuropathology					

ATTACHMENT 5

SUMMARY OF DIETARY EXPOSURE ASSESSMENTS

ATTACHMENT 5. SUMMARY OF DIETARY EXPOSURE ASSESSMENTS

	CHEMICAL PC CODE	MAJOR AG CHEMICAL	APPLICATION RATE [LBS/A]	FREQUENCY OF APPLICATION	RANGE OF ESTABLISHED TOLERANCES [PPM] (METABOLITES)	USED ON FOODS HIGHLY CONSUMED BY INFANTS and CHILDREN? YES Major Foods	USED ON FOODS HIGHLY CONSUMED BY INFANTS and CHILDREN? NO	SYSTEMIC RESIDUES	RESIDUE DATA SOURCES	RANGE and FREQ. of POSITIVE RESIDUE FINDINGS	DRES ANALYSES ACUTE	DRES ANALYSES CHRONIC
1	**ACEPHATE** 103301	✔	0.2 -1	1-6 /year	0.02-15 (Acephate per se)	beans, milk, soybeans		✔	Field Studies FDA PDP	Many detects; 0.004 - 2.4ppm	Tolerance Levels	Field Trial Data with % CT
2	**AZINPHOS-METHYL** 058001	✔	0.5 - 2	1-12 for some uses freq. not specified	0.04 - 10	apples, peaches, pears, tomatoes, milk			Field Studies FDA PDP	PDP: 42-55% apples 20-33% peaches 4.6% tomatoes 2.5% grapes 0.01 - 0.72 ppm	Tolerance Levels (Monte Carlo unacceptable)	Field Trial Data with % CT; Monitoring Data
3	**BENSULIDE** 009801 (Herbicide)		3-12.5	1 per season	0.1 - 0.15 (+ Oxygen analog)	carrots, fruiting vegetables		✔	Field Studies		Tolerance Levels	Tolerance Levels
4	**CADUSAFOS** 128864	✔ (Non-US)	Import tolerance for bananas		0.01	bananas		✔	Field Studies FDA	No detects in monitoring data.	Tolerance Levels	Tolerance Levels; Field Trial Data (½LOD); %CT
5	**CHLORETHOXYFOS** 129006		2.5-3.25	1 per season	0.01		✔		Field Studies		Tolerance Levels	Tolerance Levels

ATTACHMENT 5. SUMMARY OF DIETARY EXPOSURE ASSESSMENTS

	CHEMICAL PC CODE	MAJOR AG CHEMICAL	APPLICATION RATE [LBS/A]	FREQUENCY OF APPLICATION	RANGE OF ESTABLISHED TOLERANCES [PPM] (METABOLITES)	USED ON FOODS HIGHLY CONSUMED BY INFANTS and CHILDREN? YES Major Foods	USED ON FOODS HIGHLY CONSUMED BY INFANTS and CHILDREN? NO	SYSTEMIC RESIDUES	RESIDUE DATA SOURCES	RANGE and FREQ. of POSITIVE RESIDUE FINDINGS	DRES ANALYSES ACUTE	DRES ANALYSES CHRONIC
6	**CHLORPYRIFOS** 059101	✔	0.5-6	13 max.	0.01 - 13 (+ TCP)	apples, beans, corn, tomatoes, vegetables			Field Studies FDA PDP Market Basket Survey	PDP: ~ 10% apples (and juice), carrots, grapes, green beans, oranges, peaches, spinach, corn, peas, sweet potatoes, and tomatoes.	Monte Carlo is under review Field Trial Data with % CT	Field Trial Data with % CT
7	**CHLORPYRIPHOS-METHYL** 059102		Variable: Stored grain use		0.1 - 6.0 (TCP)	cereal grains, milk			Field Studies FDA PDP	PDP: No detectable residues (858 samples)	Not Done. In adequate tox. database.	
8	**COUMAPHOS** 036501	✔	Varies based on formulation type (dust, spray, dip).		0.5 -1 (Oxon metabolite)	milk/meat (Dermal animal applications)			Field Studies FDA		Anticipated Residues from Field Trial Data	Anticipated Residues from Field Trial Data
9	**DIAZINON** 057801	✔	0.5 - 5.0	1-6 (peaches and pears)	0.1 - 40 (diazinon oxon and hydroxy metabolite)	apples, peaches, pears, tomatoes, carrots			Field Studies FDA PDP	PDP: ~10% of apples, carrots, celery, grapes, green beans, spinach, peaches, sweet peas.	Tolerance Levels	Field Trial Data with % CT; Monitoring Data
10	**DICHLORVOS (DDVP)** 084001		2.0g/ 1000 ft^3 max.	1-7 days between treatment	0.02 - 2	cereal grains, milk, tomatoes			Field Studies FDA PDP Total Diet Study	Mostly non-detects.	Field Trial Data with % CT; Monitoring Data	Field Trial Data with % CT; Monitoring Data

ATTACHMENT 5. SUMMARY OF DIETARY EXPOSURE ASSESSMENTS

	CHEMICAL PC CODE	MAJOR AG CHEMICAL	APPLICATION RATE [LBS/A]	FREQUENCY OF APPLICATION	RANGE OF ESTABLISHED TOLERANCES [PPM] (METABOLITES)	USED ON FOODS HIGHLY CONSUMED BY INFANTS and CHILDREN? YES Major Foods	NO	SYSTEMIC RESIDUES	RESIDUE DATA SOURCES	RANGE and FREQ. of POSITIVE RESIDUE FINDINGS	DRES ANALYSES ACUTE	DRES ANALYSES CHRONIC
11	**DICROTOPHOS** 035201		0.5 max.	3-5 per season	0.05 (monocrotophos)	milk (cotton - only use)		✔	Field Studies FDA	Detections in monitoring		Tolerance Levels
12	**DIMETHOATE** 035001	✔	0.5 -4.0	1-6 per season	0.02 - 5 (omethoate)	pome fruit, cereal grains, citrus, vegetables		✔	Field Studies FDA PDP	PDP: 8-12% of apple, green bean, grape, and lettuce (max. levels were 0.6, 1.4, 0.44, and 0.96 ppm respectively).	Monitoring Data	Monitoring Data
13	**DISULFOTON** 032501	✔	0.5 - 102	1 - 4 per season	0.5 - 5.0 (sulfone, sulfoxide, and oxygen analogs)	cereals, potatoes, soybeans, vegetables		✔	Field Studies FDA PDP	FDA: some detects 0.4 ppm max.	?	Field Trial Data with % CT
14	**ETHION** 058401	✔	3.0 max.	3 max.	0.1 - 14 (oxon)	pome fruits, beans, cereal grains, citrus, milk, vegetables			Field Studies FDA PDP	PDP: 0.8% of oranges (0.038 ppm max.)	Monte Carlo Field Trial Data with % CT	Field Trial Data with % CT; Monitoring Data
15	**ETHOPROP** 041101		3-12	1/year except peanuts, pineapple & turf	0.02 - 0.2 (SME, OME, M1)	bananas		✔	Field Studies		Monte Carlo is under review; Anticipated Residues from Field Trial Data	Anticipated Residues from Field Trial Data with %CT

ATTACHMENT 5. SUMMARY OF DIETARY EXPOSURE ASSESSMENTS

	CHEMICAL PC CODE	MAJOR AG CHEMICAL	APPLICATION RATE [LBS/A]	FREQUENCY OF APPLICATION	RANGE OF ESTABLISHED TOLERANCES [PPM] (METABOLITES)	USED ON FOODS HIGHLY CONSUMED BY INFANTS and CHILDREN? YES Major Foods	USED ON FOODS HIGHLY CONSUMED BY INFANTS and CHILDREN? NO	SYSTEMIC RESIDUES	RESIDUE DATA SOURCES	RANGE and FREQ. of POSITIVE RESIDUE FINDINGS	DRES ANALYSES ACUTE	DRES ANALYSES CHRONIC
16	**ETHYL PARATHION** 057501	✔	0.4 - 1.0	2-6 per season	0.05 - 20 (paraoxon and in animal commodities, 4-acetamidopara-oxon)	cereal grains, soybeans			Field Studies FDA PDP	Detects in wheat and barley.	Tolerance Levels	Field Trial Data with % CT; Monitoring Data
17	**FENAMIPHOS** 100601	✔	3	1-4 every 30 days	0.02 - 1.5 (sulfoxide and sulfone)	citrus, pome fruits, peaches, bananas, grapes, raisins		✔	Field Studies FDA PDP	PDP: No detectable residues (4830 samples; 11 crops)	Monte Carlo	Anticipated Residues from Field Trial Data with %CT
18	**FENITROTHION** 105901		Import tolerance for wheat glutan		15		✔	✔	Field Studies		Tolerance Levels	Tolerance Levels
19	**FENTHION** 053301		Varies based on formulation type (pour-on, eartag)		0.01 - 0.1 (oxygen analog, sulfoxides and sulfones)	milk crop tolerances to be revoked			Feeding Study		Extrapolation from <1x feeding study.	
20	**FONOFOS** 041701	CANCELLATION PROCEEDINGS: 6(F) BEING DRAFTED										
21	**ISAZOPHOS-METHYL** 295900	NO DATA AVAILABLE										

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ATTACHMENT 5. SUMMARY OF DIETARY EXPOSURE ASSESSMENTS

	CHEMICAL PC CODE	MAJOR AG CHEMICAL	APPLICATION RATE [LBS/A]	FREQUENCY OF APPLICATION	RANGE OF ESTABLISHED TOLERANCES [PPM] (METABOLITES)	USED ON FOODS HIGHLY CONSUMED BY INFANTS and CHILDREN? YES Major Foods	USED ON FOODS HIGHLY CONSUMED BY INFANTS and CHILDREN? NO	SYSTEMIC RESIDUES	RESIDUE DATA SOURCES	RANGE and FREQ. of POSITIVE RESIDUE FINDINGS	DRES ANALYSES ACUTE	DRES ANALYSES CHRONIC
22	ISOFENPHOS 109401	CURRENTLY NO REGISTERED USES ON AGRICULTURAL FOOD CROPS. (Ornamental lawn and turf, shrubs/trees, outdoor commercial nurseries.)										
23	MALATHION 057701	✔	0.01-6.0	1-2 week intervals; also PH use	0.1 - 135 (maloxon)	cereal grains, citrus, pome fruits, stone fruit, grapes, milk, potatoes, tomatoes, vegetables			Field Studies FDA PDP Food Contam.	10-70% of small grains (and flour) at 0.06 -0.2ppm.	Monte Carlo	Field Trial Data with % CT; Monitoring Data
24	METHAMIDOPHOS 101201	✔	0.75-1.0	4-9 per season	0.1 - 1	potatoes, tomatoes		✔	Field Studies PDP	See acephate.	Not available.	Not available.
25	METHIDATHION 100301	✔	0.4-5		0.05 - 12	citrus, pome fruit, stone fruit, potatoes			Field Studies PDP		Tolerance Levels; Monitoring Data	Tolerance Levels with %CT
26	METHYL PARATHION 053501	✔	0.2-3.0	3-8 per season	0.1 - 5	berries, cereal grains, citrus, pome fruits, stone fruits, soybeans, tomatoes, vegetables			Field Studies FDA PDP	PDP: 21-31% of peaches (0.69 ppm max); 5-7% of apples (0.083ppm max.)	Field Trial Data with % CT	Field Trial Data with % CT

ATTACHMENT 5. SUMMARY OF DIETARY EXPOSURE ASSESSMENTS

	CHEMICAL PC CODE	MAJOR AG CHEMICAL	APPLICATION RATE [LBS/A]	FREQUENCY OF APPLICATION	RANGE OF ESTABLISHED TOLERANCES [PPM] (METABOLITES)	USED ON FOODS HIGHLY CONSUMED BY INFANTS and CHILDREN? YES Major Foods	USED ON FOODS HIGHLY CONSUMED BY INFANTS and CHILDREN? NO	SYSTEMIC RESIDUES	RESIDUE DATA SOURCES	RANGE and FREQ. of POSITIVE RESIDUE FINDINGS	DRES ANALYSES ACUTE	DRES ANALYSES CHRONIC
27	**NALED** 034401		0.02-3.6	3/year except mosquito use	0.05 - 10 (conversion product, DDVP)	citrus, other fruits, squash/melons, peas, beans, soybeans			Field Studies FDA		Anticipated Residues from Field Trial Data (Monte Carlo unacceptable)	Anticipated Residues from Field Trial and Processing Study Data
28	**ODM** 058702		0.5 (typical)	2-3 per season	0.1 - 12.5 (in plants, ODMS)	citrus, grapes, pome fruits, stone fruits, squash/melons, beans, corn, potatoes		✔	Field Studies	Detectable residues in whole fruits and leafy vegetables.	Tolerance Levels	Field Trial Data with % CT
29	**PHORATE** 057201		1-4	1 per season	0.05 - 3 (sulfoxide, sulfone, and oxygen analogs)	cereal grains, milk, sugarcane, soybeans		✔	Field Studies FDA PDP	PDP: No detectable residues (4831 samples)	Monte Carlo	Tolerance Levels with %CT
30	**PHOSMET** 059201	✔	0.7-6	10 max. (cotton); 6 max. (apples)	0.1 - 40 (oxon)	citrus, grapes, nuts, pome fruits, peaches, corn potatoes, peas, sweet potatoes			Field Studies FDA PDP	PDP: 27% of peaches; <6% of sweet potatoes, green beans, apples (and juice); No detects in oranges, corn, tomatoes or milk.	Tolerance Levels	Field Trial Data with % CT; Monitoring Data
31	**PHOSTEBUPIRIM (TEBUPIRIMFOS)** 129086		7.3 max.	1 per season	0.01	corn			Field and Processing Studies	No detectable residues.	Tolerance Levels	Tolerance Levels

ATTACHMENT 5. SUMMARY OF DIETARY EXPOSURE ASSESSMENTS

	CHEMICAL PC CODE	MAJOR AG CHEMICAL	APPLICATION RATE [LBS/A]	FREQUENCY OF APPLICATION	RANGE OF ESTABLISHED TOLERANCES [PPM] (METABOLITES)	USED ON FOODS HIGHLY CONSUMED BY INFANTS and CHILDREN? YES Major Foods	NO	SYSTEMIC RESIDUES	RESIDUE DATA SOURCES	RANGE and FREQ. of POSITIVE RESIDUE FINDINGS	DRES ANALYSES ACUTE	DRES ANALYSES CHRONIC
32	**PIRIMIPHOS-METHYL** 108102		Variable: Stored grain use; also eartag		0.2 - 88	grain, milk			Field Studies FDA	FDA: real residues found in stored grain.	Tolerance Levels	Field Trial Data with % CT
33	**PROFENOPHOS** 111401	25% of cotton crop	0.025-1.0	6lbs per season max.	0.01 - 2; 55 (gintrash)	milk cotton - only use			Field Studies		Tolerance Levels	Field Trial Data with % CT
34	**PROPETAMPHOS** 113601	CURRENTLY NO REGISTERED USES ON AGRICULTURAL FOOD CROPS. (REFS: Pets; indoor/outdoor household dwellings; food processing, handling and storage plants/areas; eating establishments; food marketing, storage and distribution facilities; commercial storages or warehouses.)										
35	**SULFOTEPP** 079501	NO DATA AVAILABLE										
36	**TEMEPHOS** 059001 (Larvicide)	CURRENTLY NO REGISTERED USES ON AGRICULTURAL FOOD CROPS. (Public health chemical - mosquito larvicide)										
37	**TERBUFOS** 105001	✔	1.3-4.4	1/year	0.025 - 0.5 (oxygen analog, sulfoxides and sulfones)	bananas, corn		✔	Field Studies FDA PDP	No detectable residues for corn or sorghum. Banana field trials: detects at 0.01-0.025ppm	Monte Carlo	Field Trial Data with % CT

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ATTACHMENT 5. SUMMARY OF DIETARY EXPOSURE ASSESSMENTS

	CHEMICAL PC CODE	MAJOR AG CHEMICAL	APPLICATION RATE [LBS/A]	FREQUENCY OF APPLICATION	RANGE OF ESTABLISHED TOLERANCES [PPM] (METABOLITES)	USED ON FOODS HIGHLY CONSUMED BY INFANTS and CHILDREN? YES Major Foods	USED ON FOODS HIGHLY CONSUMED BY INFANTS and CHILDREN? NO	SYSTEMIC RESIDUES	RESIDUE DATA SOURCES	RANGE and FREQ. of POSITIVE RESIDUE FINDINGS	DRES ANALYSES ACUTE	DRES ANALYSES CHRONIC
38	**TETRACHLORVINPHOS** 083701		Varies based on formulation type (emulsifiable concentrate, dust, granular, wettable powder).		0.05 - 7	milk (Dermal and feed through animal applications)			RED is requiring Magnitude of the Residue Studies.		Not required.	Anticipated Residues based on Metabolism Studies (% livestock treated)
39	**TRIBUFOS (DEF)** 074801 (Defoliant)	✔	1.3 -1.9	1-2 per season	0.02 - 4	milk			FDA	Found detects at LOD (meat and milk)	Tolerance Levels	Tolerance Levels with %CT
40	**TRICHLORFON** 057901		8.0 max. (turf)	not specified	0.01 - 60	bananas, beans, carrots, cereal grains, citrus, corn, milk		✔	Field Studies		Tolerance Levels	Anticipated Residues from Field Trial Data

ATTACHMENT 6

SUMMARY OF DRINKING WATER EXPOSURE ASSESSMENTS

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ATTACHMENT 6.	SUMMARY OF DRINKING WATER EXPOSURE ASSESSMENTS								
	CHEMICAL PC CODE	ENVIRONMENTAL FATE DATABASE COMPLETE?		COMPOUND (or Degradate) IS A LEACHER?		RELIABLE STUDIES AVAILABLE FOR EECs? (Conducted in vulnerable areas at max label rate)		EECs BASED ON MODELING? Model and Tier		POTENTIAL POPULATION EXPOSED
		YES	NO Cite Major Deficiencies	YES	NO	GROUND WATER	SURFACE WATER	GROUND WATER	SURFACE WATER	
1	**ACEPHATE** 103301	✔*	* Lacking acceptable acrobic aquatic metabolism data.	✔		No	No	SCI-GROW Tier 1	GENEEC Tier 1	Widely used. EECs include Methamidophos. PRZM/EXAMS (Tier 2) in progress.
2	**AZINPHOS-METHYL** 058001	✔			✔	No	No	SCI-GROW Tier 1	PRZM/EZAMS Tier 2	Exposure is unlikely to the majority of the population. Small watersheds in high use areas (cotton fields and apple/fruit orchards) may be exposed seasonally through surface water runoff. Chronic exposures are not expected to exceed HED's levels of concern for drinking water (DWLOCs). Acute exposures at levels of concern may occur in the spring.
3	**BENSULIDE** 009801		✔		✔	No	No	SCI-GROW Tier 1	PRZM/EZAMS Tier 2	Since bensulide binds to organic matter and will be found predominately associated with suspended sediments in the water column, standard coagulation-flocculation and sedimentation processes should be effective in removing it from drinking water.
4	**CADUSAFOS** 128864	No domestic uses, therefore no potential for water contamination.								
5	**CHLORETHOXYFOS** 129006	✔			✔	No	No	SCI-GROW Tier 1	PRZM/EZAMS Tier 2	Corn use - terrestrial food
6	**CHLORPYRIFOS** 059101	✔			✔	USGS monitoring data	Samples taken from streams; not "targeted"	SCI-GROW Tier 1	GENEEC Tier 1 PRZM/EZAMS Tier 2	Extensive termiticide use and much ag use. Assessment used both monitoring and modeling.

ATTACHMENT 6. SUMMARY OF DRINKING WATER EXPOSURE ASSESSMENTS

	CHEMICAL PC CODE	ENVIRONMENTAL FATE DATABASE COMPLETE?		COMPOUND (or Degradate) IS A LEACHER?		RELIABLE STUDIES AVAILABLE FOR EECs? (Conducted in vulnerable areas at max label rate)		EECs BASED ON MODELING? Model and Tier		POTENTIAL POPULATION EXPOSED
		YES	NO Cite Major Deficiencies	YES	NO	GROUND WATER	SURFACE WATER	GROUND WATER	SURFACE WATER	
7	**CHLORPYRIPHOS-METHYL** 059102	No drinking water exposure assessment done. Stored grain use is not likely to result in water contamination.								
8	**COUMAPHOS** 036501	✔		✔		EECs were not calculated for Coumaphos. Drinking water exposure was not assessed.				Contamination of drinking water is unlikely. Dermal animal use only.
9	**DIAZINON** 057801		✔Several fate studies in house that require review.	✔		No	No	To be conducted.	To be conducted.	Used throughout the environment. About half is used on lawns with the remaining used on both crop and non-crop commodities. Exposure potential is considered highly likely to all populations.
10	**DDVP (DICHLORVOS)** 084001	✔		✔		No	No	SCI-GROW Tier 1	GENEEC Tier 1	
11	**DICROTOPHOS** 035201		Some of the fate studies may need to be repeated.	✔		No Detects in STORET - under review.	No	SCI-GROW Tier 1	GENEEC Tier 1	Exposure is limited to areas where cotton is grown.
12	**DIMETHOATE** 035001		Lacking metabolites, sorption/desorption, and field dissipation data.	✔		No	No	SCI-GROW Tier 1	PRZM/EZAMS Tier 2	Potential for large portion of population to be exposed since use is wide spread (indoor non-ag. and food uses).
13	**DISULFOTON** 032501		✔		✔	Some (not targeted)	No	SCI-GROW Tier 1	PRZM/EZAMS Tier 2	Used modeling and some ground monitoring.

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ATTACHMENT 6.	SUMMARY OF DRINKING WATER EXPOSURE ASSESSMENTS								
	CHEMICAL PC CODE	ENVIRONMENTAL FATE DATABASE COMPLETE?		COMPOUND (or Degradate) IS A LEACHER?		RELIABLE STUDIES AVAILABLE FOR EECs? (Conducted in vulnerable areas at max label rate)		EECs BASED ON MODELING? Model and Tier		POTENTIAL POPULATION EXPOSED
		YES	NO Cite Major Deficiencies	YES	NO	GROUND WATER	SURFACE WATER	GROUND WATER	SURFACE WATER	
14	**ETHION** 058401		Lacking metabolites, sorption/desorption, and field dissipation data.		✔	No	Yes	SCI-GROW Tier 1	PRZM/EZAMS Tier 2 Not Used	Used on 40-60% of all citrus (major use). Surface water modeling performed but not used in assessment.
15	**ETHOPROP** 041101	✔			✔	No	No	SCI-GROW Tier 1	PRZM/EZAMS Tier 2	Extensive.
16	**ETHYL PARATHION** 057501		✔	✔		No	No	SCI-GROW Tier 1	PRZM/EZAMS Tier 2	Although use is limited (9 crops), the fact that it is used almost all over the U.S. indicates considerable potential for exposure.
17	**FENAMIPHOS** 100601		✔	✔		Yes	No	No	GENEEC Tier 1 PRZM/EZAMS Tier 2	Residents of CA, TX, MD, OR, NJ and the southeast (especially FL) who live in agricultural areas and consume water obtained from domestic wells.
18	**FENITROTHION** 105901	No drinking water exposure assessment done. Very limited use (greenhouses and some hand spraying ornamental trees in nurseries) is not likely to result in water contamination.								
19	**FENTHION** 053301	✔			✔	No	No	SCI-GROW Tier 1	PRZM/EZAMS Tier 2	Limited exposure expected due to limited use pattern.
20	**FONOFOS** 041701	CANCELLATION PROCEEDINGS: 6(f) BEING DRAFTED.								

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ATTACHMENT 6.	SUMMARY OF DRINKING WATER EXPOSURE ASSESSMENTS								
	CHEMICAL PC CODE	ENVIRONMENTAL FATE DATABASE COMPLETE?		COMPOUND (or Degradate) IS A LEACHER?		RELIABLE STUDIES AVAILABLE FOR EECs? (Conducted in vulnerable areas at max label rate)		EECs BASED ON MODELING? Model and Tier		POTENTIAL POPULATION EXPOSED
		YES	NO Cite Major Deficiencies	YES	NO	GROUND WATER	SURFACE WATER	GROUND WATER	SURFACE WATER	
21	ISAZOPHOS-METHYL 295900	NO DATA AVAILABLE.								
22	ISOFENPHOS 109401	✔			✔	No	No	SCI-GROW Tier 1	GENEEC Tier 1	Limited exposure expected due to limited use pattern (lawns and golf courses).
23	MALATHION 057701		✔	✔		Yes	No	No	GENEEC Tier 1	Widely used - potential for low exposures to many populations. Highest exposures expected in areas treated by aerial application for mosquito and medfly control.
24	METHAMIDOPHOS 101201	✔*	* Lacking acceptable aerobic aquatic metabolism data.	✔		No	No	SCI-GROW Tier 1	GENEEC Tier 1	Widely used. PRZM/EXAMS (Tier 2) in progress.
25	METHIDATHION 100301		Data gaps exist for the identification, accumulation and decline of metabolites in the aerobic soil metabolism and field dissipation studies	✔		No	No	SCI-GROW Tier 1	GENEEC Tier 1 PRZM/EZAMS Tier 2	Because of many label uses, the exposure could be extensive.

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ATTACHMENT 6.	SUMMARY OF DRINKING WATER EXPOSURE ASSESSMENTS								
	CHEMICAL PC CODE	ENVIRONMENTAL FATE DATABASE COMPLETE?		COMPOUND (or Degradate) IS A LEACHER?		RELIABLE STUDIES AVAILABLE FOR EECs? (Conducted in vulnerable areas at max label rate)		EECs BASED ON MODELING? Model and Tier		POTENTIAL POPULATION EXPOSED
		YES	NO Cite Major Deficiencies	YES	NO	GROUND WATER	SURFACE WATER	GROUND WATER	SURFACE WATER	
26	**METHYL PARATHION** 053501		✔		✔	Yes: USGS NAWQA study but not "targeted"	Yes	SCI-GROW Tier 1	GENEEC Tier 1 PRZM/EZAMS Tier 2	Potential rare acute exposure possible for populations deriving drinking water from surface-water sources. Monitoring data used for characterization.
27	**NALED** 034401	✔			✔	No	No	SCI-GROW Tier 1	PRZM/EZAMS Tier 2	
28	**ODM** 058702		✔		✔	No	No	SCI-GROW Tier 1	PRZM/EZAMS Tier 2	
29	**PHORATE** 057201	✔	✔Lacking environmental fate data on sulfoxide and sulfone metabolites.	✔		No	No	SCI-GROW Tier 1	PRZM/EZAMS Tier 2	Extensive: It is used on corn as an at-plant insecticide. The degradates are more mobile and persistent than the parent.
30	**PHOSMET** 059201	✔			✔	Non-targeted studies - consistent with modeling.	Yes	SCI-GROW Tier 1	PRZM/EZAMS Tier 2	Extensive.
31	**PHOSTEBUPIRIM (TEBUPIRIMFOS)** 129086		Unresolved issues associated with field dissipation studies.	✔		No	No	SCI-GROW Tier 1	GENEEC Tier 1	Because of use on corn, the exposure could be extensive.

ATTACHMENT 6.	SUMMARY OF DRINKING WATER EXPOSURE ASSESSMENTS								
	CHEMICAL PC CODE	ENVIRONMENTAL FATE DATABASE COMPLETE?		COMPOUND (or Degradate) IS A LEACHER?		RELIABLE STUDIES AVAILABLE FOR EECs? (Conducted in vulnerable areas at max label rate)		EECs BASED ON MODELING? Model and Tier		POTENTIAL POPULATION EXPOSED
		YES	NO Cite Major Deficiencies	YES	NO	GROUND WATER	SURFACE WATER	GROUND WATER	SURFACE WATER	
32	**PIRIMIPHOS-METHYL** 108102	No drinking water exposure assessment done. Stored grain and cattle eartag uses are not likely to result in water contamination.								
33	**PROFENOPHOS** 111401	✔*	* Fate of profenofos under acidic conditions is uncertain.	✔		No	No	SCI-GROW Tier 1	GENEEC Tier 1	Uncertain; potentially confined to cotton-growing region, primarily in the southeastern U.S.
34	**PROPETAMPHOS** 113601	No drinking water exposure assessment done. Pet and indoor uses are not likely to result in water contamination.								
35	**SULFOTEPP** 079501	No drinking water exposure assessment done. Greenhouse use is not likely to result in water contamination.								
36	**TEMEPHOS** 059001	No drinking water exposure assessment done. Public health chemical - application is restricted to guard against drinking water contamination.								
37	**TERBUFOS** 105001	✔*	* Complete for parent. Incomplete for sulfoxide and sulfone degradates.	✔		Yes: For the parent compound in corn.	Yes: For the parent compound in corn.	SCI-GROW Tier 1	PRZM/EZAMS Tier 2	EECs are derived from a combination of monitoring and modeling. Because of use on corn, the exposure could be extensive.
38	**TETRACHLORVINPHOS** 083701	No drinking water exposure assessment done. Animal feed through and dermal applications are not likely to result in water contamination.								

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ATTACHMENT 6.	SUMMARY OF DRINKING WATER EXPOSURE ASSESSMENTS								
	CHEMICAL PC CODE	ENVIRONMENTAL FATE DATABASE COMPLETE?		COMPOUND (or Degradate) IS A LEACHER?		RELIABLE STUDIES AVAILABLE FOR EECs? (Conducted in vulnerable areas at max label rate)		EECs BASED ON MODELING? Model and Tier		POTENTIAL POPULATION EXPOSED
		YES	NO Cite Major Deficiencies	YES	NO	GROUND WATER	SURFACE WATER	GROUND WATER	SURFACE WATER	
39	TRIBUFOS (DEF) 074801		Lacking metabolites, sorption/desorption, and field dissipation data.		✔	Yes EPA PGWDB (No detects in 569 wells)	No	SCI-GROW Tier 1	PRZM/EZAMS Tier 2	Limited exposure expected due to limited use pattern (cotton defoliant).
40	TRICHLORFON 057901	✔		✔		No	No	SCI-GROW Tier 1	PRZM/EZAMS Tier 2	

ATTACHMENT 7

SUMMARY OF RESIDENTIAL EXPOSURE ASSESSMENTS

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ATTACHMENT 7.	SUMMARY OF RESIDENTIAL EXPOSURE ASSESSMENTS									
	CHEMICAL PC CODE	RESIDENTIAL USES	CHEMICAL SPECIFIC DATA?		PHED DATA USED?		DRAFT SOPs USED for POST-APPLICATION RESIDENTIAL EXPOSURE?		OTHER MODELS USED	BIOMONITORING DATA AVAILABLE or INCIDENTS REPORTED?	DERMAL ABSORP-TION
			YES	NO	YES	NO	YES (Deviations)	NO			
1	**ACEPHATE** 103301	Lawns Ornamentals Crack & Crevice	✔		✔No data for some scen-arios.		✔		None		Dermal study
2	**AZINPHOS-METHYL** 058001	No residential uses.									
3	**BENSULIDE** 009801	Lawns Ornamentals		✔	✔		✔			"Very few incidents reported. None confirmed.".	100%
4	**CADUSAFOS** 128864	No residential uses.									
5	**CHLORETHOXYFOS** 129006	No residential uses.									

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ATTACHMENT 7.	SUMMARY OF RESIDENTIAL EXPOSURE ASSESSMENTS									
	CHEMICAL PC CODE	RESIDENTIAL USES	CHEMICAL SPECIFIC DATA?		PHED DATA USED?		DRAFT SOPs USED for POST-APPLICATION RESIDENTIAL EXPOSURE?		OTHER MODELS USED	BIOMONITORING DATA AVAILABLE or INCIDENTS REPORTED?	DERMAL ABSORP-TION
			YES	NO	YES	NO	YES (Deviations)	NO			
6	**CHLORPYRIFOS** 059101	Lawns Ornamentals Fruit Trees Vegetable Gardens Pets Crack & Crevice Termiticide	✔ Post-application study from registrant for indoor broadcast treatments (dermal only; no data for hand-to-mouth exposure)			✔		✔	Exposure Factors Handbook .		1%
7	**CHLORPYRIPHOS-METHYL** 059102	No residential uses.									
8	**COUMAPHOS** 036501	No residential uses.									
9	**DIAZINON** 057801	Lawns Ornamentals Fruit Trees Vegetable Gardens Pets Foggers Crack & Crevice		✔	✔		✔		None		100% assumed

ATTACHMENT 7.	SUMMARY OF RESIDENTIAL EXPOSURE ASSESSMENTS									
	CHEMICAL PC CODE	RESIDENTIAL USES	CHEMICAL SPECIFIC DATA?		PHED DATA USED?		DRAFT SOPs USED for POST-APPLICATION RESIDENTIAL EXPOSURE?		OTHER MODELS USED	BIOMONITORING DATA AVAILABLE or INCIDENTS REPORTED?	DERMAL ABSORP-TION
			YES	NO	YES	NO	YES (Deviations)	NO			
10	**DICHLORVOS (DDVP)** 084001	Lawns Pets Foggers Crack & Crevice Pest Strips	✔ Post-application study using Jazzercise® Model		✔			✔	Two separate literature studies were used for dislodgeable residue data and exposure data for resin strips	Biomonitoring data is included in chemical specific exposure study	11% (or used biomonitoring data)
11	**DICROTOPHOS** 035201	No residential uses.									
12	**DIMETHOATE** 035001	Ornamentals	✔ Poor quality data: not used		✔		Post-application exposure calculations were deferred (pending negotiations with registrant addressing concerns with handler risk assessments).	✔	None		11%
13	**DISULFOTON** 032501	Ornamentals Indoor Plants		✔	✔		✔		Post-application Surrogate Spreadsheet	PCC (1982-89): ranked 11th among the 28 chemicals reported (Occupational)	
14	**ETHION** 058401	No residential uses.									

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	CHEMICAL PC CODE	RESIDENTIAL USES	CHEMICAL SPECIFIC DATA?		PHED DATA USED?		DRAFT SOPs USED for POST-APPLICATION RESIDENTIAL EXPOSURE?		OTHER MODELS USED	BIOMONITORING DATA AVAILABLE or INCIDENTS REPORTED?	DERMAL ABSORP-TION
			YES	NO	YES	NO	YES (Deviations)	NO			
15	**ETHOPROP** 041101	No residential uses.									
16	**ETHYL PARATHION** 057501	No residential uses.									
17	**FENAMIPHOS** 100601	No residential uses.									
18	**FENITROTHION** 105901	Ant and roach bait stations	No residential exposure assessment done. Low potential for exposure from enclosed bait stations.								
19	**FENTHION** 053301	No Residential Uses	PHED and the Residential SOPs were used to assess post-application exposure following aerial and ground ULV mosquito abatement treatments.						Ag DRIFT Model Tier III	PCC (1985-92): ranked 3rd or 4th in the child catagories of % hospitalized, % with symptoms, and % life threatening symptoms	20%
20	**FONOFOS** 041701	CANCELLATION PROCEEDINGS: 6(f) BEING DRAFTED.									
21	**ISAZOPHOS-METHYL** 295900	No residential uses.									

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ATTACHMENT 7.	SUMMARY OF RESIDENTIAL EXPOSURE ASSESSMENTS									
	CHEMICAL PC CODE	RESIDENTIAL USES	CHEMICAL SPECIFIC DATA?		PHED DATA USED?		DRAFT SOPs USED for POST-APPLICATION RESIDENTIAL EXPOSURE?		OTHER MODELS USED	BIOMONITORING DATA AVAILABLE or INCIDENTS REPORTED?	DERMAL ABSORPTION
			YES	NO	YES	NO	YES (Deviations)	NO			
22	**ISOFENPHOS** 109401	Lawns		✔	✔		✔		None	PCC (1985-92): 351 cases reported; 110 incidents involved children ≤ age 5	100% assumed
23	**MALATHION** 057701	Lawns Ornamentals Fruit Trees Vegetable Gardens		✔	✔No data for some scen-arios		✔		AgDRIFT Model - to estimate post-application dermal exposure following aerial applications for mosquito control	"Still in Review"	Route specific endpoints
24	**METHAMIDOPHOS** 101201	No residential uses.									
25	**METHIDATHION** 100301	No residential uses.									
26	**METHYL PARATHION** 053501	No Residential Uses *Reported incidents are probably due to a canceled use (professional application to residential fruit trees)								*12 incidents in IDS; 274 cases in Poison Control Center data; 26 cases in children ≤ age 5	

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ATTACHMENT 7.	SUMMARY OF RESIDENTIAL EXPOSURE ASSESSMENTS									
	CHEMICAL PC CODE	RESIDENTIAL USES	CHEMICAL SPECIFIC DATA?		PHED DATA USED?		DRAFT SOPs USED for POST-APPLICATION RESIDENTIAL EXPOSURE?		OTHER MODELS USED	BIOMONITORING DATA AVAILABLE or INCIDENTS REPORTED?	DERMAL ABSORP-TION
			YES	NO	YES	NO	YES (Deviations)	NO			
27	**NALED** 034401	Lawns Ornamentals Fruit Trees Vegetable Gardens Pets		✔	✔No data for some scen-arios.		Post-application exposure assessment not completed for uses with no data (including pet collars or back pack sprayer).	✔	None	REFS: 48 incidents reports including fieldworkers, pet casualties and others.	100% assumed
28	**ODM** 058702	No residential uses.									
29	**PHORATE** 057201	No residential uses.									
30	**PHOSMET** 059201	Ornamentals Fruit Trees Vegetable Gardens Pets	✔		✔		✔ assuming monthly applications; residue dissipation rate of 1% used on treated pets		None	Incidents have been reported associated with pet use.	10%
31	**PHOSTEBUPIRIM (TEBUPIRIMFOS)** 129086	No residential uses.									
32	**PIRIMIPHOS-METHYL** 108102	No residential uses.									

ATTACHMENT 7.	SUMMARY OF RESIDENTIAL EXPOSURE ASSESSMENTS										
	CHEMICAL PC CODE	RESIDENTIAL USES	CHEMICAL SPECIFIC DATA?		PHED DATA USED?		DRAFT SOPs USED for POST-APPLICATION RESIDENTIAL EXPOSURE?		OTHER MODELS USED	BIOMONITORING DATA AVAILABLE or INCIDENTS REPORTED?	DERMAL ABSORP-TION
			YES	NO	YES	NO	YES (Deviations)	NO			
33	PROFENOPHOS 111401	No residential uses.									
34	PROPETAMPHOS 113601	Pets (REFS) Foggers Crack & Crevice Termiticide	Residential exposure assessment has not been completed - incomplete tox database. Expect PHED and the Residential SOPs to be used.								
35	SULFOTEPP 079501	No residential uses.									
36	TEMEPHOS 059001	No residential uses.									
37	TERBUFOS 105001	No residential uses.									
38	TETRACHLORVINPHOS 083701	Pets Pet Quarters		✔	✔		✔ Frequency of applications were estimated by staff.		None		9.57%
39	TRIBUFOS (DEF) 074801	No residential uses.									

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	CHEMICAL PC CODE	RESIDENTIAL USES	CHEMICAL SPECIFIC DATA?		PHED DATA USED?		DRAFT SOPs USED for POST-APPLICATION RESIDENTIAL EXPOSURE?		OTHER MODELS USED	BIOMONITORING DATA AVAILABLE or INCIDENTS REPORTED?	DERMAL ABSORP-TION
			YES	NO	YES	NO	YES (Deviations)	NO			
40	TRICHLORFON 057901	Lawns Ornamentals Pets Crack & Crevice	Residential exposure assessment has not been completed. Expect PHED and the Residential SOPs to be used.								

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