



013731-3
UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF
PREVENTION PESTICIDES AND
TOXIC SUBSTANCES

August 31, 1999

MEMORANDUM

SUBJECT: **PHORATE:** Revised HED Chapter of the Reregistration Eligibility Decision Document (RED), Case #0103, PC Code 057201; Barcode No. D259262

From: Christine L. Olinger, Chemist
Reregistration Branch 1
Health Effects Division 7509C

A handwritten signature in black ink, likely belonging to Christine L. Olinger, is written over the typed name and title.

Thru: Whang Phang, Ph.D., Branch Senior Scientist
Reregistration Branch 1
Health Effect Division 7509C

A handwritten signature in black ink, likely belonging to Whang Phang, is written over the typed name and title.

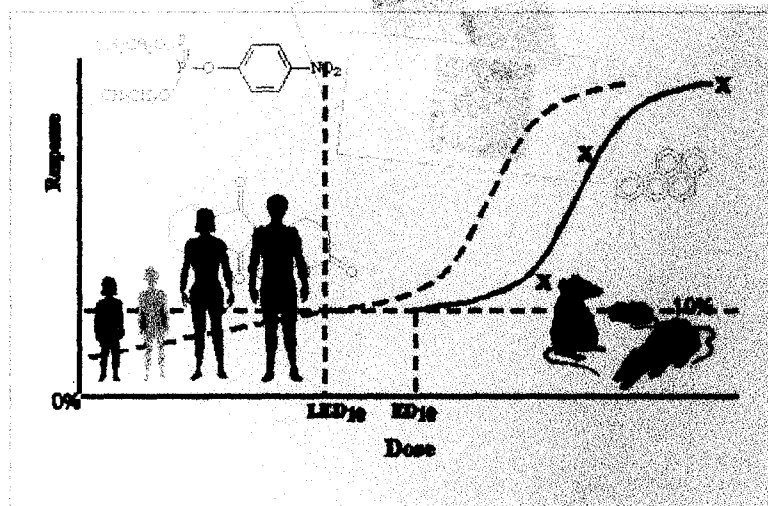
To: Ben Chambliss/Stephanie Willett
Reregistration Branch I
Special Review and Reregistration Division 7508W

Attached is the revised Health Effects Division (HED) chapter to the Phorate RED. Please let us know if you have any further questions.

cc: MHawkins (for Caswell, microfiche), COlinger (RRB1), JDawson (RRB1)

HUMAN HEALTH RISK ASSESSMENT

PHORATE



U.S. Environmental Protection Agency
Office of Pesticide Programs
Health Effects Division (7509C)
Christine L. Olinger, Risk Assessor

September 2, 1999

HUMAN HEALTH RISK ASSESSMENT

Phorate

Phase 5

Risk Assessment Team:

Lead Risk Assessor:

Christine L. Olinger, Chemist

Dietary Risk:

David J. Miller, Chemist

Christina Swartz, Chemist

Christine L. Olinger, Chemist

Occupational and

Jeff Dawson, Chemist

Residential Exposure:

Epidemiology:

Jerome Blondell, Ph.D, Epidemiologist

Toxicology:

Yung Yang, PhD., Toxicologist

Elizabeth Mendez, Ph.D., Toxicologist

Management:

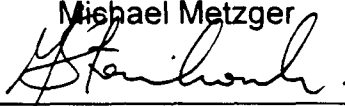
Senior Scientist:

Whang Phang, Ph.D.

Branch Chief:

Michael Metzger

Division Director:


Margaret J. Stasikowski, Date

Introduction

New toxicity and exposure studies have been received and reviewed since the previous version of the phorate risk assessment. Comments received from USDA, the registrant, grower groups, and other interested parties have been incorporated into the revised assessment.

This revision incorporates the results of the new rat acute neurotoxicity study and new dietary risk analyses conducted by the Agency using DEEM™. We have also added a summary of considerations used in the acute and chronic dietary risk analyses which describes the use patterns which result in the residues upon which the assessment is based. The acute dietary risk summary table includes the results of DEEM analyses in which specific commodities were moved in order to determine which uses significantly contribute to the acute risk.

The occupational exposure and risk assessment consider a new subchronic dermal toxicity study on rats using a granular formulation; an occupational exposure study conducted with a similar chemical, terbufos, reflecting loading with a closed loading system and varying levels of PPE; and an occupational risk assessment prepared by the registrant.

EXECUTIVE SUMMARY

The Health Effects Division (HED) has evaluated the phorate data base and determined that the data are adequate to support reregistration. The toxicological data base is adequate to support reregistration, although some data gaps exist. Residue chemistry data requirements are substantially complete.

Phorate, is an organophosphate insecticide used on many crops. Phorate is manufactured and sold in the United States by American Cyanamid Corporation.

Hazard Assessment

The toxicology data base provides strong evidence confirming that phorate, like other organophosphates, has anticholinesterase activity in all species tested, including hen, mice, rats, dogs and rabbits. By the oral, inhalation, and dermal routes technical phorate is placed in Toxicity Category I. No acceptable data are available on the eye and dermal irritation because of the high acute toxicity which prohibits the administration of appropriate dose levels. Inhibition of plasma, erythrocyte and/or brain cholinesterase (ChE) activity occurs by all routes (oral, dermal and inhalation) and duration (acute, subchronic, and chronic) of exposures. Phorate did not produce delayed neurotoxicity in the hen.

Phorate is not a significant developmental or a reproductive toxicant. There was no evidence of increased susceptibility to rat or rabbit fetuses following *in utero* exposures or in the offsprings following pre/post natal exposure to rats. Phorate has been classified as a group E carcinogen - "not likely" to be carcinogenic to humans based on carcinogenicity studies in rats and mice.

The metabolism of phorate in rats indicates that approximately 90% of the administered dose was excreted in 72 hours and there was no significant tissue residue. Absorbed material was extensively and completely metabolized.

The FQPA Safety Factor Committee following review of the hazard and exposure data recommended that the 10x safety factor to account for enhanced sensitivity of infants and children (as required by FQPA) should be reduced to 3x, based on the lack of acute and subchronic neurotoxicity studies. The toxicity studies showed no increased susceptibility in fetuses as compared to maternal animals following *in utero* exposures in rats and rabbits and no increased sensitivity in pups when compared to adults. The acute neurotoxicity study has been received and reviewed by the Agency; the subchronic study has recently been submitted, but has not yet been reviewed. Upon review of the study, the Committee will reconsider the FQPA safety factor.

Exposure and Risk Assessments Conducted

Exposure and risk assessments were conducted for phorate as follows: acute and chronic dietary assessments to capture exposure estimates for the general public; and, dermal and inhalation exposure assessments to capture estimates for occupational exposures. Non-occupational (residential) exposure and risk assessments are not applicable since there are no registered non-occupational (residential) uses at this time.

Dietary Exposure and Risk

For the acute dietary risk assessment, the acute Population Adjusted Dose (PAD) of 0.00083 mg/kg/day was derived by the use of the No Observable Adverse Effects Level (NOAEL) of 0.25 mg/kg/day and an uncertainty factor of 300 which includes 10x for interspecies extrapolation, 10x for intraspecies variation, and the FQPA safety factor of 3. The NOAEL was based on miosis (pupil constriction) and inhibition of brain cholinesterase activity observed in the acute neurotoxicity study in rats at the Lowest Observed Adverse Effects Level (LOAEL) of 0.50 mg/kg/day.

For the chronic dietary risk assessment, the chronic Population Dose (PAD) of 0.00017 mg/kg/day was derived by the use of the NOAEL of 0.05 mg/kg/day and an uncertainty factor of 100 which includes 10x for interspecies extrapolation, 10x for intraspecies variation, and the 3x FQPA safety factor. The NOAEL was based on inhibition of red blood cell and brain cholinesterase activity observed in the chronic toxicity study in dogs at the LOAEL of 0.25 mg/kg/day.

The dietary risk analysis used food consumption data from the 1989-1992 USDA Continuing Survey of Food Intake by Individuals (CSFII) survey, information on the percent of crop treated, and data from field trial studies. FDA and USDA monitoring data showed non-detectable residues in all commodities with the exception of potatoes. **Acute and chronic dietary risk were below the Agency level of concern for all subpopulations.**

Occupational Exposure and Risk

For dermal exposures of less than 28 days, the dermal risk assessment is based on a NOAEL of 0.41 mg/kg/day from a subchronic dermal exposure study with a phorate granular formulation on rats. Red blood cell and brain cholinesterase inhibition were

observed at the next highest dose level, 0.81 mg/kg/day. For dermal exposures exceeding 28 days, and inhalation exposures exceeding seven days, the Agency relied upon the one-year dog study previously described. For inhalation exposures of less than seven days, the Agency used the acute rat neurotoxicity described in the previous section. The Agency used the oral exposure studies when route-specific studies (dermal and inhalation) of an appropriate duration were not available, and assumed equivalent toxicity compared to the oral route (i.e. 100% dermal and inhalation absorption).

The Agency used an occupational exposure study submitted by the registrant for occupational scenarios reflecting closed loading systems and varying levels of personal protective equipment. Data from the Agency's occupational exposure database, PHED, were used for all other scenarios.

The occupational risk assessment showed that occupational risk did not exceed the Agency's level of concern when closed loading systems (commonly known as "Lock 'n Load" systems) and personal protective equipment (PPE) were used. If minimal personal protective equipment, open cabs, and products are loaded using bags that must be ripped open prior to loading, then risks exceed the Agency's level of concern. At this time some labels do not require the use of PPE and closed loading systems.

Table of Contents - Phorate HED Chapter

A. Physical and Chemical Properties Assessment	
1. Identification of Active Ingredient	1
2. Manufacturing Use Products	1
B. Human Risk Assessment	
1. Hazard Assessment	
a. Acute Toxicity	3
b. Subchronic Toxicity	4
c. Chronic Toxicity and Carcinogenicity	5
d. Developmental Toxicity	6
e. Reproductive Toxicity	7
f. Mutagenicity	7
g. Metabolism	8
h. Neurotoxicity	9
i. Dermal Toxicity and Absorption	10
j. Other Toxicological Considerations	10
2. Dose Response Assessment	
a. Special Sensitivity to Infants and Children	11
b. Chronic Reference Dose (RfD)	12
c. Carcinogenic Classification and Risk Quantification	12
d. Developmental Classification	12
e. Dermal Absorption	12
f. Other Toxicological Endpoints	
i. Acute Dietary	12
ii. Short and Intermediate Term Occupational and Residential (Dermal and Inhalation)	13
iii. Chronic Occupational and Residential (Non-Cancer)	13
iv. Inhalation (Any Time Period)	13
3. Dietary Exposure and Risk Assessment/Characterization	
a. Dietary Exposure (Food Sources)	
i. 860.1200 Directions for Use	15
ii. 860.1300 Nature of the Residue - Plants	16
iii. 860.1300 Nature of the Residue - Livestock	16
iv. 860.1340 Residue Analytical Methods	17
v. 860.1360 Multiresidue Methods	17
vi. 860.1380 Storage Stability Data	18
vii. 860.1500 Crop Field Trials	18
viii. 860.1520 Processed Food/Feed	19
ix. 860.1480 Meat, Milk, Poultry, and Eggs	20
x. 860.1400 Water, Fish, and Irrigated Crops	20
xi. 860.1460 Food Handling Establishments	20
xii. 860.1850 Confined Accumulation in Rotational Crops	20
xiii. 860.1900 Field Accumulation in Rotational Crops	21
xiv. Tolerance Reassessment Table	21
xv. Codex Harmonization	25

b.	Dietary Exposure (Drinking Water Source)	
i.	Groundwater	27
ii.	Surface Water	28
c.	Dietary Risk Assessment and Characterization	
i.	Chronic Risk	28
ii.	Acute Dietary Risk	29
iii.	Drinking Water Risk (Acute and Chronic)	35
4.	Occupational and Residential Exposure and Risk Assessment/Characterization	
a.	Occupational and Residential Exposure	37
i.	Summary of Use Patterns and Formulations	37
ii.	Mixer/Loader/Applicator Exposure Assessment	37
iii.	Post-Application Exposure Assessment	41
b.	Occupational and Residential Risk Assessment and Characterization	
i.	Risk from Dermal and Inhalation Exposure	44
ii.	Incident Reports	44
iii.	Occupational Risk Characterization	45
c.	Statement of the Adequacy of the Residential Exposure Database to Assess Infant and Child Exposure	50
5.	Aggregate Exposure and Risk Assessment/Characterization	
a.	Acute Aggregate Exposure and Risk	50
b.	Chronic Aggregate Exposure and Risk	50
References		50

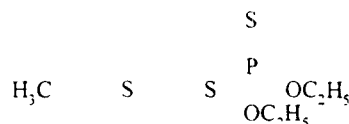
Tables and Figures

Table 1.	Acute Toxicity Values for Technical Phorate	3
Table 2.	Summary of Toxicological Endpoints for Phorate	14
Table 3.	Phorate End-use Products	15
Table 4.	Tolerance Reassessment Summary	23
Table 5.	Codex MRLs and Applicable U.S. Tolerances	26
Table 6.	Results of Chronic Dietary Risk Analysis for Phorate	29
Table 7.	Summary of Considerations Used in the Acute and Chronic Dietary Risk Analyses	31
Table 8.	Results of Acute Dietary Exposure/Risk Analyses for Phorate	34
Table 9.	DWLOCs for Chronic and Acute Exposure to Phorate	36
Table 10.	Summary of Application Assumptions	41
Table 11.	Summary of Daily Occupational Exposures for Application to Peanuts	42
Table 12.	Summary of Occupational Risk Estimates	47
Figure A.	Chemical Structures of Phorate Residues of Concern	17

A. Physical and Chemical Properties Assessment

- Description of Chemical

Phorate [O,O-diethyl S[(ethylthio)methyl]phosphorodithioate] is a soil and systemic insecticide.



Empirical Formula: $\text{C}_7\text{H}_{17}\text{O}_2\text{PS}_3$
 Molecular Weight: 260.4
 CAS Registry No.: 298-02-2
 PC Code No.: 057201

- Identification of Active Ingredient

Technical phorate is a colorless to light yellow clear liquid with a boiling point of 118-120 C. Phorate is slightly soluble in water at 20-50 ppm and soluble in most organic solvents, such as acetone and xylene. It is miscible in alcohols, ethers, ketones, esters, carbon tetrachloride, and vegetable oils. Phorate is subject to hydrolysis under alkaline conditions, but is stable under neutral and acidic conditions.

- Manufacturing-use Products

A search of the Reference Files System (REFS) conducted 8/99 identified three phorate manufacturing-use products (MPs) registered under PC Code No. 057201: the American Cyanamid 85% technical and 85% formulation intermediate (T and FI; EPA Reg. Nos. 241-213 and 241-212, respectively), and the Aceto Agricultural Chemicals Corporation 85% T (EPA Reg. No. 2749-106). We note that although REFS lists label claims of 85% for all three products, the American Cyanamid products are properly identified as 92% formulations (CBRS No. 13228, D199207, 8/24/95, K. Dockter), and Aceto has agreed to modify the label claim to 95% for its technical product (CBRS No. 16229, D219423, 10/6/95, D. Miller). Only the American Cyanamid and Aceto phorate MPs are subject to a reregistration eligibility decision.

The product chemistry data requirements for the American Cyanamid 92% T and 92% FI (EPA Reg. Nos. 241-213 and 241-212, respectively) and the Aceto Agriculture

Chemicals Corporation 95% FI (EPA Reg. No. 2749-106) phorate are all fulfilled. Provided that the registrants either certify that the suppliers of beginning materials and the manufacturing processes for the phorate Ts and FI have not changed since the last comprehensive product chemistry review or submit complete updated product chemistry data packages, HED has no objections to the reregistration of phorate with respect to product chemistry data requirements.

B. Human Risk Assessment

1. Hazard Assessment

a. Acute Toxicity

There are few new acute toxicity studies available for phorate. Essentially all the acute toxicity studies were previously reviewed and published in the Registration Standard for phorate (December, 1988). The acute toxicity database is adequate for phorate. Table 1 summarizes acute toxicity values and categories for phorate.

Table 1. Acute Toxicity Values for Technical Phorate¹

Study	Results	Category
Oral LD ₅₀ - Rat	3.7 mg/kg (M), 1.4 mg/kg (F)	I
Dermal LD ₅₀ - Rat	9.3 mg/kg (M), 3.9 mg/kg (F)	I
Inhalation LC ₅₀ - Rat	0.06 mg/L (M), 0.011 mg/L (F)	I
Eye Irritation	Waived ²	N/A
Dermal Irritation	Waived ²	N/A
Dermal Sensitization	Waived ²	N/A

¹ Data are excerpted from the Pesticide Registration Standard for Phorate (Dec. 1988)(p. 8-9).

² High acute toxicity prohibits administration of appropriate dose levels.

Technical phorate is highly toxic on an acute oral, dermal, and inhalation basis. The oral LD₅₀ values for phorate with rats were 3.7 and 1.4 mg/kg in males and females, respectively (Toxicity Category I). All of the animals that died in this study showed typical clinical signs of cholinergic toxicity such as salivation, lacrimation, exophthalmos, muscle fasciculation and excessive urination and defecation (US EPA, 1988; Newell and Dilley, 1978; MRID# 00126343; satisfies Guideline 870.1100).

The dermal LD₅₀ values for phorate with rats were 9.3 and 3.9 mg/kg in males and females, respectively (Toxicity Category I). The cholinergic signs noted for the acute oral study were also observed in the acute dermal study (US EPA, 1988; Newell and Dilley, 1978; MRID# 00126343; satisfies Guideline 870.1200). In addition, a dermal LD₅₀ of 415.6 mg/kg in guinea pigs with typical cholinergic signs noted at higher doses was also reported (Shaffer, 1960; Baron, 1968; MRID# 00139479).

The acute inhalation LC₅₀s for rats were 0.06 and 0.011 mg/L for males and females, respectively (Toxicity Category I), based on a one-hour exposure to analytical grade

phorate aerosol. Typical cholinergic signs were observed in intoxicated animals (US EPA, 1988; Newell and Dilley, 1978; MRID# 00126343; satisfies Guideline 870.1300).

There were no acceptable data available on the primary eye or dermal irritation properties of phorate. However, these tests were waived since the high acute toxicity of phorate prohibits the administration of appropriate dosage levels. Likewise, no data are available on the primary dermal sensitization properties of phorate. This study was waived because of the high acute toxicity of phorate (US EPA, 1988).

b. Subchronic Toxicity

There were data available from a 90-day feeding study in rats and a 105-day feeding study in dogs (MRID# 00092873). These studies were conducted in 1956 and were classified as supplementary since the protocols did not adhere to the current guidelines. However, because the toxicity endpoint (cholinesterase inhibition) was satisfactorily identified, and because sufficient data from chronic toxicity studies in rodents and non-rodents were available, additional data from subchronic toxicity studies are not required. Executive summaries of these two studies follow.

In a 90-day feeding study in rats (Tusing, 1956; MRID# 0092873), phorate was administered in the diet at dosage levels of 0, 0.22, 0.66, 2.0, 6.0, 12.0 or 18.0 ppm (equivalent to 0, 0.011, 0.033, 0.1, 0.3, 0.6, and 0.9 mg/kg/day, respectively) for 90 days. Phorate at 12 and 18 ppm induced mortality as well as reduced body weight gains and food consumption (both sexes). RBC ChE activity was inhibited in females at 2.0 ppm while plasma, RBC and brain ChE activities were inhibited in both sexes at the 6.0 ppm level. The NOAEL was 0.66 ppm (0.033 mg/kg/day) and the LOAEL was 2 ppm (0.1 mg/kg/day) based on plasma cholinesterase inhibition. The study was classified as supplementary because the histopathology was performed on only 3 (not 10) rats/sex.

In a 105-day feeding study in dogs (Tusing, 1956; MRID# 0092873), technical phorate was administered in capsules to dogs at dosages of 0, 0.01, 0.05, 0.25, 1.25, or 2.5 mg/kg/day, 6 days/week for 13-15 weeks. Each group had 3 dogs (two males and one female) with the exception of the 2.5 mg/kg group, which had two males only. The plasma ChE activity was inhibited at a dose of 0.05 mg/kg/day or above (combined sexes). The RBC ChE was inhibited at a dose of 0.25 mg/kg/day or above (combined sexes). All dogs at the 1.25 and 2.5 mg/kg/day levels showed typical cholinergic signs and subsequently died. The NOAEL was 0.01 mg/kg/day and the LOAEL was 0.05 mg/kg/day based on the reduction of plasma ChE activity. This study was classified as supplementary because only three dogs (two males and one female) per group were used instead of four dogs of each sex per group (8 dogs total).

In a 21/28-day dermal toxicity study, 3 groups of Sprague-Dawley CD® rats (10/sex/group) received topical applications of granular phorate (20.30%) at 0, 2, 4, and 15 mg/kg/day. (The dose level of the highest dose group was reduced to 10 mg/kg/day during the last week of the study.) The dosages based on the active ingredient (a.i.) are 0.406, 0.812, and 3.05/2.03 mg/kg/day (females) or 4.06/3.05 mg/kg/day males. The test animals were exposed to phorate for 6 hours/day, 5 days/week, for 4 weeks. Significant plasma (PChE), red blood cell (RChE), and brain (BChE) cholinesterase activity inhibition was seen in both males and females at the high-dose level. The extent of PChE, RChE, and BChE inhibition was 23 - 61% , 64 -76%, and 41%, respectively for males; and 66 - 91%, 53 - 97%, and 68%, respectively for females. A small but statistically-significant decrease in RChE and BChE was also observed in females at the 4 mg/kg/day dose level during week 4 of the study. Significant mortality (5/10) was seen in the high dose female group during the first 3 weeks of the study. The test article, however, did not appear to have an impact on the survival of males. Signs of cholinergic toxicity such as lacrimation, ano-genital staining, lethargy, tremors, irregular gait, labored breathing were observed in 6 high dose females from days 9-25 of the study. Of these 6 animals, 3 were found dead before the end of the study period. Under the conditions of this study, the LOAEL is established at 4 mg/kg/day (0.812 mg/kg/day a.i.) based on evidence of statistically-significant decreases in PChE, RChE, and BChE activity in females. The NOAEL is established at 2 mg/kg/day (0.406 mg/kg/day a.i.). (Compton 1999, MRID No. 44794201, satisfies Guideline 870.3200)

c. Chronic Toxicity and Carcinogenicity

In a combined two-year chronic toxicity/carcinogenicity study in rats (50/sex/group), phorate was administered in the diet (50/sex/group) at dosage levels of 0, 1, 3, or 6 ppm (equivalent to 0, 0.05, 0.15, and 0.3 mg/kg/day, respectively) for 24 months. A NOAEL for plasma ChE inhibition in males was not established since the LOAEL was 0.05 mg/kg/day, the lowest dose tested (LDT). The NOAEL for plasma ChE inhibition in females was 0.05 mg/kg/day while the LOAEL was 0.15 mg/kg/day. The NOAEL for RBC ChE inhibition was 0.3 mg/kg/day (highest dose tested (HDT)) in males and 0.15 mg/kg/day in females while the LOAEL for females was 0.3 mg/kg/day. The NOAEL for brain ChE inhibition was 0.15 mg/kg/day in males and 0.05 mg/kg/day in females while the LOAELs were 0.3 and 0.15 mg/kg/day for males and females, respectively. The high dose level tested was considered adequate for carcinogenicity testing. Phorate was not considered carcinogenic under the conditions of the study because the treatment did not alter the spontaneous tumor profile in rats (Manus et al., 1981; MRID# 00125233; satisfies Guidelines 870.4300).

In a chronic toxicity study, groups of beagle dogs (6/sex/group) were administered phorate via capsules at doses of 0, 0.005, 0.01, 0.05, or 0.25 mg/kg/day for one year. Compound related effects included slight body tremors in high dose males and females and marginal inhibition of body weight gain in high dose males. The systemic NOAEL

was 0.05 mg/kg/day and the LOAEL was 0.25 mg/kg/day based on body tremors in males and females and inhibited body weight gains in males. The NOAEL for plasma ChE inhibition was 0.01 mg/kg/day while the LOAEL was 0.05 mg/kg/day for both sexes. The NOAEL for RBC or brain ChE inhibition was 0.05 mg/kg/day while the LOAEL was 0.25 mg/kg/day for both sexes (Shellenberger and Tegeris, 1987; MRID# 40174527; satisfies Guideline 870.4100).

In a carcinogenicity study, groups of CD-1 mice (50/sex/group) received phorate at a dietary concentration of 0, 1, 3, or 6 ppm (equivalent to 0, 0.15, 0.45, and 0.9 mg/kg/day) for 78 weeks. There were no consistent toxic signs or any non-neoplastic pathologic findings related to test compound administration. The NOAEL was 0.45 mg/kg/day and the LOAEL was 0.9 mg/kg/day based on a slight decrease in weight gain in females in the first 25 weeks. The dose level tested was considered adequate for carcinogenicity testing based on the results of the range finding study. The treatment did not alter the spontaneous tumor profile in this strain of mice (Manus et al. 1981; MRID# 00124845; satisfies Guideline 870.4200).

d. Developmental Toxicity

Technical phorate in corn oil was administered by oral intubation to pregnant rats (23 female/group) from day 6 to day 15 of gestation at dosages of 0, 0.125, 0.25, or 0.5 mg/kg/day. No developmental effects were observed in this study at any dosage. The NOAEL for both maternal toxicity and developmental toxicity was 0.25 mg/kg/day. The LOAEL for each was 0.5 mg/kg/day in which dams exhibited increased mortality, convulsions, and hypothermia while the fetuses showed enlarged hearts. The enlargement of the heart was considered to be a physiologic effect as a result of increased acetylcholine, producing excessive stimulation of the myocardium with ensuing enlargement (Beliles, 1979; MRID# 00122775; satisfies Guideline 870.3700).

Groups of pregnant rabbits (20/group) were administered 0, 0.15, 0.5, 0.9 or 1.2 mg/kg/day of phorate by gavage on days 6-18 of gestation. The maternal NOAEL was 0.15 mg/kg/day and the maternal LOAEL was 0.5 mg/kg/day based on body weight loss and increased mortality. The developmental NOAEL was 1.2 mg/kg/day (the highest dose tested). No developmental effects were observed (Schroeder, 1987; MRID# 40174528; satisfies Guideline 870.3700).

In a developmental toxicity study, pregnant Crl:CD®BR rats (24-25/dose) received oral administration of Phorate (92.1%) in corn oil at dose levels of 0, 0.1, 0.2, 0.3 or 0.4 mg/kg/day from days 6 through 15 of gestation. For maternal toxicity, the NOAEL was 0.3 mg/kg/day and the LOAEL was 0.4 mg/kg/day, based on increased mortality, clinical signs indicative of neurotoxicity, decreases in body weight and body weight gain and food consumption and gross pathology. Developmental toxicity was manifested as decreased fetal weights and increased incidence of skeletal variations (delayed

ossification of the sternum and pelvis). For developmental toxicity, the NOAEL was 0.3 mg/kg/day and LOAEL was 0.4 mg/kg/day (Lochry, 1990; MRID No. 44422301; satisfies Guideline 870.3700).

e Reproductive Toxicity

There was a 3-generation reproductive study in mice (1965; MRID# 00092853) submitted to the Agency. In this study, technical phorate was administered in the diet to mice at dietary levels of 0, 0.6, 1.5 or 3.0 ppm (equivalent to 0, 0.09, 0.23, and 0.45 mg/kg/day, respectively). Compound administration was initiated 7 weeks before the first mating. The study involved 3 generations with 2 litters (a and b) per generation. The only apparent indications of reproductive toxicity were slight reductions in the lactation and viability indices in the F₁b at the highest dose level. The NOAEL was estimated to be 1.5 ppm (0.23 mg/kg/day) and the LOAEL was 3.0 ppm (0.45 mg/kg/day) based on effects on viability and lactation indices. This 3-generation reproduction study was down-graded from core minimum to unacceptable by the HED/RfD Peer Review Committee (December 30, 1993).

In a two-generation reproduction study, groups of male and female Sprague-Dawley rats (25/sex) were fed diets containing Phorate (92.1%) at dose levels of 0, 1, 2, 4, or 6 ppm (0, 0.087, 0.176, 0.359 or 0.603 mg/kg/day for males and 0, 0.103, 0.210, 0.420 or 0.727 mg/kg/day for females) for two successive generations. For parental systemic toxicity, the NOAEL was 0.2 mg/kg/day and the LOAEL was 0.4 mg/kg/day based on clinical signs (tremors) and inhibitions of plasma and brain cholinesterase activity (F₁ females only). For offspring toxicity, the NOAEL was 0.2 mg/kg/day and the LOAEL was 0.4 mg/kg/day based on decreased pup survival and pup body weight. The decrease in pup survival was seen during early lactation and the decrease in pup body weights was seen during the later part of lactation (Schroeder, 1991; MRID No. 44422302; satisfies Guideline 870.3800).

f. Mutagenicity

Sufficient data are available to satisfy data requirements for mutagenicity testing. Technical phorate did not induce a genotoxic response in any of the tests listed below.

- Gene mutation assays -

In an Ames assay, phorate was negative at dosages up to 1000 µg/plate with Salmonella typhimurium strains TA100, TA 1535, TA 1537, and TA 1538 in the presence and absence of metabolic activation (Simmon et al., 1977; MRID# 00124901).

A test for reverse mutation in Escherichia coli was negative at dosages up to 1000 µg/plate in the presence and absence of metabolic activation (Simmon et al., 1977; MRID# 00124901).

Phorate did not induce gene mutations at the HGPRT locus in cultured Chinese hamster ovary (CHO) cells at dosages up to 100 nL/mL with and without metabolic activation (Thilagar et al., 1985; MRID# 00151633).

- Chromosomal aberration assays-

A dominant lethal test in mice was negative at dosages up to 20 mg/kg in the diet (Simmon et al., 1977; MRID# 00124901)

A chromosomal aberrations test was negative in mammalian (rats) bone marrow cells at ip (intraperitoneal) dosages up to 2.5 and 1.5 mg/kg in males and females, respectively (Ivett, 1986; MRID# 00155597).

- Other genotoxic effects studies -

Negative in mitotic recombination assay with Saccharomyces cerevisiae D3 at a concentration of 5% with and without metabolic activation (Simmon et al., 1977; MRID# 00124901).

Preferential toxicity assays in DNA repair-proficient and -deficient strains of Escherichia coli and Bacillus subtilis at a level of 1000 µg/plate were negative (Simmon et al., 1977; MRID# 00124901).

Preferential toxicity assays in DNA repair-proficient and -deficient strains of Bacillus subtilis (strain H17 and M45, respectively) at 1000 µg/plate were negative (Simmon et al., 1977; MRID# 00124901).

Unscheduled DNA synthesis (UDS) assay in human fibroblasts (WI-38 cells) at concentrations up to 10^{-3} M (Mol/L) did not show mutagenic response (Simmon et al., 1977; MRID# 00124901).

g. Metabolism

Data are available from rat metabolism studies in males and females. A single oral dose of 0.8 mg/kg ^{14}C -phorate was administered to male rats. The chemical was readily absorbed and excreted, with approximately 77.2% of the total administered ^{14}C in the urine and 11.7% in the feces within 24 hours. Less than 1% of the total radioactivity was found in tissues (highest level in blood) at 24 hours. Ten metabolites were present in the urine. Two non-phosphorylated metabolites, ethyl (methyl sulfinyl) methyl-sulfone and (ethyl sulfonyl)(methyl-sulfonyl) methane, comprised approximately 71% of the radioactivity present in the urine. About 9% and 10% of the urinary ^{14}C was associated with (O,O-diethyl S-(ethyl sulfonyl) methyl phosphorothioic acid and [(ethyl sulfinyl) methyl, methyl sulfone], respectively. Unchanged parent compound accounted for only 0.5% of the recovered urinary ^{14}C and the remaining four phosphorylated

compounds plus one unidentified metabolite together comprised less than 10% of the urinary radioactivity. These metabolites were formed following cleavage of the sulfur-phosphorus bond associated with the carbon chain in phorate, from methylation of the liberated thiol group, and from oxidation of the resulting sulfide to sulfoxide and sulfone (Hussain, 1987; MRID# 40291601).

Female rats showed a comparable pathway to that described for males (Miller and Wu, 1991; MRID# 41803803).

h. Neurotoxicity

In a delayed neurotoxicity study, 14.2 mg/kg (LD₅₀ dose) of phorate was administered orally to hens followed by a 21-day interval and a second administration at the same dosage level. Phorate did not cause neurological changes indicative of delayed neurotoxicity (US EPA, 1988; Fletcher, 1984; MRID# 00152640; Guideline 870.6100).

In an acute neurotoxicity study, 4 groups of 7 week old Sprague-Dawley CD® rats (20/sex/group) were given a single oral dose (by gavage) of phorate (91.8% a.i.) in corn oil at doses of 0, 0.25, 0.50, or 1.0 mg/kg of body weight. The first indication of a compound-related effect (miosis) detected by the FOB was reported at the 0.5 mg/kg (2/10 males and 2/10 females) and 1.0 mg/kg (2/10 males and 5/10 females) doses approximately 4-5 hours after exposure to the test substance (time of peak effect). In addition to miosis, one female at the 1.0 mg/kg dose level showed evidence of slight tremors, fasciculations, slightly impaired locomotion, and splayed/dragging hindlimbs. Another female in this dose group also exhibited moderate tremors. These symptoms resolved within the first week and were no longer evident at the Day 8 observation period. Significant cholinesterase activity inhibition in plasma, red blood cells, and the brain was seen in both males and females at the 1.0 mg/kg dose level. A small but statistically-significant decrease in brain cholinesterase activity (6%) was also observed in males at the 0.5 mg/kg dose level. Under the conditions of this study, the LOAEL is established at 0.50 mg/kg/day based on the evidence of miosis and of statistically-significant brain acetylcholinesterase inhibition in males. The NOAEL is 0.25 mg/kg/day. (Mandella 1998; MRID# 44719901, satisfies Guideline 870.6200).

A subchronic neurotoxicity study on phorate was recently submitted to the Agency, but has not yet been evaluated at this time.

The data from has received a developmental toxicity study in rats and a 2-generation reproduction toxicity study in rats that does not show increased susceptibility for infants and children exposed to phorate. In addition, these studies do not demonstrate any findings indicative of effects on the developing nervous system. Although this would provide support for not requiring a developmental neurotoxicity study, it was noted that histopathological evaluation of perfused tissue in rats was not available in the data

base. Due to concerns regarding the potency of this chemical, and in the absence of this histopathological data, the Hazard Identification Assessment Review Committee (HIARC), at the February 3, 1998 meeting decided to place the requirement for a developmental neurotoxicity study under reserve status pending receipt and evaluation of the acute and subchronic neurotoxicity studies.

i. Dermal Absorption

No dermal absorption studies are available. The dermal absorption is considered to be 100% for the purposes of risk assessment because the chemical is very acutely toxic (Tox Category I) by either oral or dermal administration (Toxicology Endpoint Selection Committee meeting of 1/23/96, and confirmed by the HIARC 12/3/98).

j. Other Toxicological Considerations

No data are available on the eye effects of phorate in specialized acute and subchronic studies. The Toxicology Chapter of the Registration Standard for Phorate (December, 1988) indicated that additional specialized studies are required to determine the potential for phorate to induce adverse ocular effects in acute and subchronic studies in rats and a six month study in dogs, rabbits, or monkeys. The Agency has determined that these studies are no longer required, based on the recommendation of the FIFRA Scientific Advisory Panel (SAP) that these studies should not be routinely required for organophosphate pesticides (March 1997).

In a 90-day feeding study, phorate sulfoxide (a phorate metabolite) was administered to rats (35/sex) at dietary levels of 0, 0.32, 0.8 or 2.0 ppm (equivalent to 0, 0.016, 0.04, and 0.10 mg/kg, respectively). Sporadic inhibition of RBC and plasma ChE activity was observed in females at the 0.8 ppm level. At 2.0 ppm, RBC, plasma, and brain ChE activities were inhibited in females while only marginal inhibition of RBC and plasma ChE activity was noted in males. No other dosage-related adverse effects were reported in this study. The NOAEL was 0.32 ppm (0.016 mg/kg) and the LOAEL was 0.8 ppm (0.04 mg/kg) based on inhibition of plasma and RBC ChE activities (Hutchison et al., 1968; MRID# 00092912).

Another phorate metabolite, (ethylsulfonyl) (methylsulfonyl) methane, has an acute oral LD₅₀ value of greater than 5000 mg/kg. In addition, this phorate metabolite does not have the structural properties of a cholinesterase inhibitor. Therefore, this phorate metabolite is not expected to be an acute toxicological concern (Lowe and Fischer, 1987, MRID# 40174526).

Phorate can be metabolized to more potent anticholinesterase compounds through oxidative desulfuration and/or sulfide oxidation. The oxidation products include the sulfoxide and sulfone derivatives of phorate and a phorate oxygen analogue. Findings

of the rat metabolism study showed that the oxidized, phosphorylated products represented minor proportions of the phorate metabolites measured in tissues, feces, and urine. Although the phorate sulfoxide metabolite appears to be slightly more toxic than the parent (as demonstrated above in the 90-day rat study with the metabolite) both compounds are very toxic and there is not much difference in their relative toxicity. For this reason, all of the data supporting phorate are adequate to support the metabolites which also inhibit cholinesterase. The Agency reserves the option to require additional toxicity studies with the oxidized metabolites if significant residue levels are detected.

2. Dose Response Assessment

a. Special Sensitivity to Infants and Children

On February 3, 1998 the Hazard Identification Assessment Review Committee (HIARC) met to evaluate the toxicology database and determine whether sufficient information was available to assess enhanced sensitivity of infants and children exposed to phorate. The developmental toxicity studies showed no increased susceptibility in fetuses as compared to maternal animals following *in utero* exposures in rats and rabbits. Similarly, the two-generation reproduction toxicity study in rats showed no increased sensitivity in offspring when compared to adults. However, the Committee determined that the **10x** factor to account for enhanced sensitivity of infants and children (as required by FQPA) **should be reduced to 3x** (instead of 1x) because of neurotoxicity data gaps. At the time of meeting, no acute, subchronic, and developmental neurotoxicity studies had been submitted. As explained in the previous section on neurotoxicity, the HIARC decided to reserve the requirement for a developmental neurotoxicity study pending submission of the acute and subchronic studies. Accordingly, data on cholinesterase inhibition, neurobehavioral effects (FOB) and histopathology on the central and peripheral nervous system were not available for evaluation after repeated exposures to phorate. The Committee also determined that a MOE (Margin of Exposure) of 300 is required for the protection of the general population including infants and children from dietary and residential exposure to phorate. This decision was confirmed in meeting of the Committee comparing all organophosphate pesticides (July, 1998).

Since the time of the decision on the FQPA safety factor, the acute neurotoxicity study has been submitted and evaluated by the Agency. The registrant very recently submitted the subchronic neurotoxicity study. Upon completion of the Agency review of the subchronic study, the FQPA Committee will reconsider the safety factor for phorate.

b. Chronic Reference Dose

The HED Hazard Identification Assessment Review Committee (HIARC) established a chronic RfD of 0.0005 mg/kg/day from a one-year feeding study in dogs and an uncertainty factor of 100 to account for differences among species and variability among humans. The FQPA factor was reduced to 3 (instead of 1) because of the subchronic neurotoxicity data gap. Therefore the chronic Population Adjusted Dose (cPAD) is 0.00017 mg/kg/day. The NOAEL in the one-year feeding study in dogs was 0.05 mg/kg/day and the LOAEL was 0.25 mg/kg/day based on body tremors and depression of RBC and brain ChE activity observed in both sexes.

It should be noted that a regulatory value (ADI) of 0.0005 mg/kg/day was established for phorate by the World Health Organization (WHO) in 1994 and verified in 1996. This value is based on a NOAEL of 0.05 mg/kg/day from a one-year dog study and an uncertainty factor of 100.

c. Carcinogenicity Classification and Risk Quantification

Phorate has been classified as a group E - "not likely" to be carcinogenic to humans based on carcinogenicity studies in rats and mice in which no treatment-related increase in tumor incidence was seen in the test animals.

d. Developmental Classification

Phorate is not considered a significant developmental toxicant.

e. Dermal Absorption

No dermal absorption studies are available. The dermal absorption is considered to be 100% for the purposes of risk assessment because the chemical is very acutely toxic (Tox Category I) by either oral or dermal administration (Toxicology Endpoint Selection Committee meeting of 1/23/96 and confirmed by the HIARC 12/3/98).

f. Other Toxicological Endpoints

A summary of all endpoints may be found in Table 2 on page 14.

i. Acute Dietary

For acute dietary risk assessment, the Health Effects Division Hazard Identification Assessment Review Committee established an acute RfD of 0.0025 mg/kg/day from an acute neurotoxicity study in rats and an uncertainty factor of 100 to account for differences among species and variability among humans. The FQPA factor was

reduced to 3 (instead of 1) because of the subchronic neurotoxicity data gap. The acute Population Adjusted Dose (aPAD) is equal to the RfD/FQPA factor, or 0.00083 mg/kg/day. The NOAEL in the acute neurotoxicity study in rats was 0.25 mg/kg/day and the LOAEL was 0.5 mg/kg/day based on miosis observed in both sexes, and a slight, but statistically-significant, decrease in brain cholinesterase activity in males.

ii. Short- and Intermediate-Term Occupational and Residential

For occupational risk assessments for time intervals of less than 28 days the HIARC recommended a dose of 0.41 mg/kg/day from a dermal toxicity study with the 20G formulation in rats (MRID 44794201), based on RBC and brain cholinesterase inhibition observed at the LOAEL of 0.81 mg/kg/day (HIARC report, 7/12/99). A Margin of Exposure of 100 is considered to be protective for all occupational assessments.

iii. Chronic Occupational and Residential (Non-Cancer)

For chronic occupational, non-cancer risk assessment, the Health Effects Division Toxicology Endpoint Selection Committee recommended an endpoint and a dose of 0.05 mg/kg/day from a one-year feeding study in dogs (MRID#40174527) based on observations of tremors and inhibition of RBC and brain ChE activities in both sexes of dogs at 0.25 mg/kg/day. This decision was later confirmed at the HIARC meeting on the endpoint selection of all organophosphate pesticides (July 8, 1998). However, since there are no chronic occupational/residential exposure scenarios, the risk assessment was not done.

iv. Inhalation (any time period)

Except for an acute inhalation toxicity study, no inhalation toxicity studies are available for selection of a dose and endpoint for a inhalation exposure risk assessment. For exposure intervals of less than seven days, an oral NOAEL of 0.25 mg/kg/day from the acute rat neurotoxicity study was selected for an inhalation risk assessment. An oral NOAEL of 0.05 mg/kg/day from the one-year dog study was selected for inhalation risk assessment for intervals exceeding one week. Oral studies were selected because of the lack of appropriate inhalation studies, and it is assumed that the inhalation absorption is 100% (default value) when calculating the exposure, i.e. inhalation toxicity is equivalent to oral toxicity.

Table 2. Summary of Toxicological Endpoints for Phorate

Exposure	Dose (Mg/kg/day)	Endpoint	Study
Acute RfD	NOAEL = 0.25	Miosis and brain cholinesterase inhibition	Acute Neurotoxicity - Rat
		UF =100 Acute RfD = 0.0025 mg/kg FQPA Population Adjusted Dose = 0.00083 mg/kg	
Chronic RfD	NOAEL = 0.05	Red blood cell and brain cholinesterase inhibition	Chronic - Dog
		UF =100 Chronic RfD = 0.0005 mg/kg/day FQPA Population Adjusted Dose = 0.00017 mg/kg/day	
Short-Term Dermal	Dermal NOAEL = 0.406	Red blood cell and brain cholinesterase inhibition	21/28-Day Dermal - Rat
Intermediate-Term Dermal ¹	Dermal NOAEL = 0.406	Red blood cell and brain cholinesterase inhibition	21/28-Day Dermal - Rat
Long-Term Dermal ²	Oral NOAEL = 0.05	Red blood cell and brain cholinesterase inhibition	Chronic - Dog
Short-Term-Inhalation ³	Oral NOAEL = 0.25	Miosis and brain cholinesterase inhibition	Acute Neurotoxicity - Rat
Intermediate-Term-Inhalation ³	Oral NOAEL = 0.05	Red blood cell and brain cholinesterase inhibition	Chronic - Dog
Long-Term Inhalation ³	Oral NOAEL = 0.05	Red blood cell and brain cholinesterase inhibition	Chronic - Dog

¹ If dermal exposure exceeds 28 days, the dose and endpoint selected for long-term dermal exposure should be used.

² 100% Dermal absorption for route-to-route extrapolation for long-term dermal exposure risk assessments.

³ 100% absorption for inhalation exposure is assumed.

3. Dietary Exposure and Risk Characterization

a. Dietary Exposure (Food Sources)

i. 860.1200 Directions for Use

A Reference Files System (REFS) search conducted 8/24/99 identified three phorate end-use products (EPs) registered to American Cyanamid Company. These EPs as well as all active Special Local Needs (SLN) registrations are listed in Table 3 below.

Table 3. Phorate End-use Products (EPs) with Food/feed Uses Registered to American Cyanamid Company and All Active SLN Registrations

EPA Reg. No. SLN No.	Acceptance Date	Formulation	Product Name
241-53	6/94	10% G	Thimet® 10-G Soil and Systemic Insecticide
241-145	4/97	15% G	Thimet® 15-G Soil and Systemic Insecticide
241-257 ¹	8/96	20% G	Thimet® 20-G Soil and Systemic Insecticide
LA920014, MT910004, OR890005, WA870010, WA910013, WI910004, ID9100014	--	20% G	Clean Crop Phorate 20 G (EPA Reg No. 34704-259)
WA920005, WI910006	--	20% G	Phorate 20-G (EPA Reg No. 9779-293)

¹ Including SLN No. LA970006.

Label amendments are required. The restriction against the feeding of treated sugar beet tops or silage to dairy cattle is considered impractical (refer to 860.1000) and should therefore be removed from labels for EPA Reg. Nos. 241-53, 241-145, and 241-257. In addition, a 30-day pregrazing interval has been established for at-cultivation applications to field corn to control chinch bug nymphs; this pregrazing interval should be extended to the at-cultivation application to field and sweet corn to control corn rootworms (EPA Reg. Nos. 241-53, 241-145, and 241-257).

In addition, a 12-month plant back restriction is appropriate for root and tuber vegetables, leafy vegetables, and cereal grains.

ii. 860.1300 Nature of the Residue - Plants

The qualitative nature of the residue in plants is adequately understood based on studies with alfalfa, beans, carrots, corn, cotton, lemons, oats, and peas. The residues of concern in plant commodities are phorate, phorate sulfoxide, phorate sulfone, phorate oxygen analog, phorate oxygen analog sulfoxide, and phorate oxygen analog sulfone. The metabolism data indicate that phorate is metabolized in plants by oxidation of the thioether sulfur and then the thiono sulfur to yield the sulfoxides and sulfones of phorate and phorate oxygen analog. Some hydrolysis of the sulfoxides and sulfones may also occur. The chemical names and structures of the residues of concern are depicted in Figure A.

The current tolerance expression is for the combined residues of phorate and its cholinesterase-inhibiting metabolites. For Codex harmonization, the tolerance expression should be revised to read as follows: the tolerances listed in 40 CFR §180.206 are established for the combined residues of the insecticide phorate (O,O-diethyl S[(ethylthio) methyl]phosphorodithioate), phorate sulfoxide, phorate sulfone, phorate oxygen analog, phorate oxygen analog sulfoxide, and phorate oxygen analog sulfone.

iii. 860.1300 Nature of the Residue - Livestock

The qualitative nature of the residue in animals is adequately understood based on the results of acceptable ruminant and poultry metabolism studies. The residues of concern in animal commodities are phorate, its oxygen analog, and their corresponding sulfoxides and sulfones. The metabolism study in *ruminants* indicates that phorate is metabolized by cleavage of the sulfur-phosphorus bond resulting in a thiolate compound which may then undergo methylation. Oxidation of the sulfur in the methylated metabolite results in various non-phosphorylated metabolites which may be further metabolized and/or incorporated into natural products. In a *poultry* metabolism study, no residues of phorate, its oxygen analog, or their sulfoxides and sulfones were detected in *poultry* tissues or eggs.

Figure A. Chemical Structures of Phorate Residues of Concern

$ \begin{array}{c} \text{S} \\ \\ \text{H}_3\text{C} - \text{S} - \text{S} - \text{P} - \text{OC}_2\text{H}_5 \\ \quad \\ \text{OC}_2\text{H}_5 \quad \text{OC}_2\text{H}_5 \end{array} $ Phorate: O,O-diethyl S-[(ethylthio)methyl] phosphorodithioate	$ \begin{array}{c} \text{O} \\ \\ \text{H}_3\text{C} - \text{S} - \text{S} - \text{P} - \text{OC}_2\text{H}_5 \\ \quad \\ \text{OC}_2\text{H}_5 \quad \text{OC}_2\text{H}_5 \end{array} $ Phorate oxygen analog: O,O-diethyl S-[(ethylthio)methyl] phosphorothioate
$ \begin{array}{c} \text{S} \\ \\ \text{H}_3\text{C} - \text{S} - \text{S} - \text{P} - \text{OC}_2\text{H}_5 \\ \quad \quad \\ \text{O} \quad \text{OC}_2\text{H}_5 \quad \text{OC}_2\text{H}_5 \end{array} $ Phorate sulfoxide: O,O-diethyl S-[(ethylsulfinyl)methyl] phosphorodithioate	$ \begin{array}{c} \text{O} \\ \\ \text{H}_3\text{C} - \text{S} - \text{S} - \text{P} - \text{OC}_2\text{H}_5 \\ \quad \quad \\ \text{O} \quad \text{OC}_2\text{H}_5 \quad \text{OC}_2\text{H}_5 \end{array} $ Phorate oxygen analog sulfoxide: O,O-diethyl S-[(ethylsulfinyl)methyl] phosphorothioate
$ \begin{array}{c} \text{S} \\ \\ \text{H}_3\text{C} - \text{S} - \text{S} - \text{P} - \text{OC}_2\text{H}_5 \\ \quad \quad \\ \text{O} \quad \text{OC}_2\text{H}_5 \quad \text{OC}_2\text{H}_5 \end{array} $ Phorate sulfone: O,O-diethyl S-[(ethylsulfonyl)methyl] phosphorodithioate	$ \begin{array}{c} \text{O} \\ \\ \text{H}_3\text{C} - \text{S} - \text{S} - \text{P} - \text{OC}_2\text{H}_5 \\ \quad \quad \\ \text{O} \quad \text{OC}_2\text{H}_5 \quad \text{OC}_2\text{H}_5 \end{array} $ Phorate oxygen analog sulfone: O,O-diethyl S-[(ethylsulfonyl)methyl] phosphorothioate

iv. 860.1340 Residue Analytical Methods - Plants and Animals

The Pesticide Analytical Manual (PAM) Volume II lists ten methods (Method I and nine "lettered" methods) for the enforcement of tolerances for phorate residues of concern in/on plant and animal commodities. Most listed methods (using GC, IR-spectroscopy, or TLC techniques) determine combined residues of phorate, phorate sulfoxide, phorate sulfone, phorate oxygen analog, phorate oxygen analog sulfoxide, and phorate oxygen analog sulfone by oxidation to phorate oxygen analog sulfone. The stated limits of detection range from 0.008 to 0.01 ppm.

Residue analytical methods for livestock commodities are no longer required because HED has recommended for revocation of animal analytical methods.

v. 860.1360 Multiresidue Methods

The FDA PESTDATA database dated 1/94 (PAM Volume I, Appendix I) indicates that phorate, phorate sulfoxide, phorate sulfone, phorate oxygen analog, phorate oxygen analog sulfoxide, and phorate oxygen analog sulfone are completely recovered (>80%) using Multiresidue method Section 302 (Luke method; Protocol D). Phorate sulfoxide,

phorate oxygen analog, phorate oxygen analog sulfoxide, and phorate oxygen analog sulfone are not recovered using Sections 303 (Mills, Onley, Gaither method; Protocol E, nonfatty) and 304 (Mills fatty food method; Protocol E, fatty). Recovery of phorate was variable and recovery of phorate sulfone was <50% using Sections 303 and 304.

vi. 860.1380 Storage Stability

Adequate storage stability data are available to support any established or reassessed tolerances in plant and animal commodities. Storage stability studies have been submitted demonstrating that residues of phorate, phorate sulfoxide, and phorate sulfone are stable for at least 2 years of frozen storage in/on dry beans, potatoes, and sugar beet roots and tops, and for at least 1.5 years in/on corn grain, forage, and fodder, and wheat grain, forage, and straw. Weathered residues of phorate were stable in corn meal and oil stored frozen for 1 year. Residues of phorate oxygen analog, phorate oxygen analog sulfoxide, and phorate oxygen analog sulfone were found to be stable for at least 2 years of frozen storage in/on dry beans. HED concludes from this information that the requirement for submission of storage stability data for phorate and its regulated sulfoxide and sulfone metabolites to support the crop field trial data is satisfied.

Storage stability data are available for milk. Phorate-related residues are stable in milk for a period of at least 4 days when stored under refrigeration and are stable for a period of at least two months when stored frozen. Since milk samples from the ruminant feeding study were stored for no longer than ca. 4-6 weeks, HED concludes that there are no storage stability concerns associated with milk. Although no storage stability studies were performed on other ruminant tissues, these samples were stored for only 4-6 weeks and HED will not require that storage stability studies be performed with these commodities.

vii. 860.1500 Crop Field Trials

The reregistration requirements for magnitude of the residue in/on coffee; field corn forage; field corn grain; sweet corn (K+CWHR); sweet corn forage; hops; peanuts; potatoes; sorghum fodder; sorghum grain; soybeans; sugar beet roots; sugar beet tops; sugarcane; wheat forage; wheat grain; and wheat straw have been satisfied. The available data indicate that the tolerance levels can be reduced for the following commodities: beans (succulent and dry); field corn grain, sweet corn (K+CWHR), potatoes, sorghum grain, soybeans, and sugarcane. The requirements for aspirated grain fractions data for field corn, sorghum, soybeans, and wheat were waived based on nondetectable residues found in/on grain/seed from field residue studies reflecting exaggerated rates.

No tolerances currently exist for field corn stover (fodder), sweet corn stover (fodder), sorghum forage, and wheat hay. Some field residue data have been submitted for these commodities; however, none of the available data reflect the currently registered use patterns for these crops. Therefore, additional field residue data are required for these commodities. In addition, Table 1 (in 860.1000 of the Residue Chemistry Guidelines, August 1996) identifies cotton gin byproducts as a raw agricultural commodity of cotton; therefore, field residue data must be submitted for cotton gin byproducts. Tolerances must be proposed for these commodities when adequate field residue data have been submitted. It is not expected that these data will significantly change the risk assessment; therefore, the data are considered confirmatory.

Food and feed additive tolerances have been proposed by IR-4 for dried and spent hops, respectively, at 2 ppm; HED previously recommended for these tolerance proposals pending submission of adequate supporting storage stability data and method validation data. Because all storage stability concerns have been resolved for phorate residues of concern, no additional data are required to support this tolerance petition. However, the petitioner should be advised that a tolerance is no longer required for spent hops and that dried hops are now considered to be a RAC; the tolerance level of 2 ppm is appropriate for dried hops.

The established tolerances for bean vines and peanut vines should be revoked since the Agency no longer considers these commodities to be significant livestock feed items (Table 1, 860.1000, August 1996). In addition, the established tolerance for peanut hay should be revoked since a restriction against the feeding of this commodity exists.

No registered uses of phorate currently exist for the following crops for which tolerances have been established: alfalfa, barley, Bermuda grass, lettuce, rice, and tomatoes. Therefore the established tolerances for these crops should be revoked.

The existing tolerances and the reassessment of these tolerances are summarized in Table 4.

viii. 860.1520 Processed Food/Feed

The reregistration requirements for magnitude of the residue in the processed commodities of coffee, cottonseed, peanuts, potatoes, sorghum, soybeans, sugar beets, sugarcane, and wheat are fulfilled.

The requirements for processing studies with cottonseed, field corn, sorghum, soybeans, and wheat were waived based on nondetectable residues found in/on grain/seed from field residue studies reflecting exaggerated rates.

The available sugar beet processing data indicate that phorate residues of concern do not concentrate in dried sugar beet pulp. Therefore, the established feed additive tolerance for this commodity should be revoked.

The existing tolerances and the reassessment of these tolerances are summarized in Table 4.

ix. 860.1480 Meat, Milk, Poultry, and Eggs

There are no registered direct animal treatments for phorate on cattle, goats, hogs, horses, sheep, or poultry. The requirements for a poultry feeding study were waived based on the results of the metabolism study. Although HED previously determined that the established tolerances for poultry commodities should remain in effect, HED now believes that given the reassessed tolerances and changes in Table 1 (860.1000, August 1996), poultry commodities can be considered to be a 180.6(a)(3) situation and current poultry and egg tolerances can be revoked.

The registrant performed a ruminant feeding study in which animals were dosed at 1.39 and 3.1 ppm; the latter value is considered to represent the maximum practical dietary burden given that greater doses resulted in clinical symptoms of organophosphate poisoning and death. Since detectable residues were not found in any ruminant tissues or milk when dosed at this maximum level, HED has concluded that a 180.6(a)(3) situation exists with respect to ruminant commodities and the current tolerances should be revoked.

x. 860.1400 Water, Fish and Irrigated Crops

Phorate is presently not registered for direct use on potable water and aquatic food and feed crops; therefore, no residue chemistry data are required under these guideline topics.

xi. 860.1460 Food-Handling Establishments

Phorate is presently not registered for use in food-handling establishments; therefore, no residue chemistry data are required under this guideline topic.

xii. 860.1850 Confined Accumulation in Rotational Crops

An adequate confined rotational crop study, reflecting plantback intervals (PBIs) of 9 and 12 months, has been submitted. Based on the results of the study, HED concluded that a 12-month plantback restriction was appropriate for root and tuber vegetables, leafy vegetables, and cereal grains but that the submitted data did not support a crop rotation restriction for peas. Additional data are required for peas.

xiii. 860.1900 Field Accumulation in Rotational Crops

Limited field rotational crop studies with peas must be submitted in order to obtain a plant-back interval. HED noted that if shorter plantback intervals were desired for root and tuber vegetables, leafy vegetables, and cereal grains, then limited field rotational crop studies would be required. There are currently no rotational crop restrictions on product labels.

The registrant subsequently submitted a confined rotational crop study reflecting a 4-month PBI to replace the 9- and 12-month PBI study. HED concluded that this study is unacceptable because the fallow land was regularly irrigated prior to planting of the rotational crops. HED required that the registrant either propose a 12-month plant back interval or submit limited field rotational crop studies at the desired plant-back interval.

xiv. Tolerance Reassessment Table

The tolerances listed in 40 CFR §180.206 are expressed in terms of phorate and its cholinesterase-inhibiting metabolites. To harmonize with the expression for Codex MRLs for residues of phorate, the tolerance expression should be revised as follows: the tolerances listed in 40 CFR §180.206 are for the combined residues of the insecticide phorate (O,O-diethyl S[(ethylthio) methyl]phosphorodithioate), phorate sulfoxide, phorate sulfone, phorate oxygen analog, phorate oxygen analog sulfoxide, and phorate oxygen analog sulfone.

Tolerances Listed Under 40 CFR §180.206:

Sufficient field trial data reflecting the maximum registered use patterns are available to ascertain the adequacy of the established tolerances for: coffee, beans, green; corn, field, forage; corn, sweet, forage; cottonseed; hops, cones, dried; peanuts; sorghum, fodder; sugar beet, roots; sugar beet, tops; wheat, forage; wheat, grain; and wheat, straw. The available data indicate that the tolerance levels can be reduced for the following commodities: beans (succulent and dry); field corn grain; sweet corn (K+CWHR); potatoes; sorghum grain; soybeans; and sugarcane.

The established tolerances for milk, eggs, and the fat, meat, and meat byproducts of cattle, goats, hogs, horses, sheep, and poultry can be revoked. HED has determined that this represents a 180.6(a)(3) situation and tolerances are not required.

The tolerance level for hops must be increased to reflect that fact that the RAC is now considered to be dried hops and not fresh hops. Adequate data are available to support a dried hops tolerance.

Because the Agency no longer considers bean vines and peanut vines to be significant livestock feed items, the established tolerances for these commodities should be revoked. The established tolerance for peanut hay should also be revoked since a restriction against the feeding of treated peanut hay exists on current product labels.

No registered uses of phorate currently exist on the following crops for which tolerances have been established: alfalfa, barley, Bermuda grass, lettuce, rice, and tomatoes. The established tolerances for the commodities of these crops should be revoked.

Sufficient data are available to assess the adequacy of the established tolerances for dried sugar beet pulp. These data indicate that phorate residues of concern do not concentrate in dried sugar beet pulp; therefore, the established feed additive tolerance should be revoked.

Tolerances To Be Proposed:

When adequate field trial data have been submitted, the registrant must propose a tolerance for field and sweet corn stover (fodder), cotton gin byproducts, sorghum forage, and wheat hay.

A summary of phorate tolerance reassessments is presented in Table 4.

Table 4. Tolerance Reassessment Summary for Phorate.			
Commodity	Current Tolerance (ppm)	Tolerance Reassessment (ppm)	Comment/ [Correct Commodity Definition]
Tolerances Listed Under 40 CFR §180.206:			
Alfalfa (fresh)	0.5	Revoke	No registered uses.
Alfalfa hay	1	Revoke	No registered uses.
Barley grain	0.1	Revoke	No registered uses.
Barley straw	0.1	Revoke	No registered uses.
Bean vines	0.5	Revoke	Not considered a significant feed item (Table 1, 860.1000).
Beans	0.1	0.05	Residues from the registered uses do not exceed the 0.05 ppm level [Beans, succulent and dry]
Bermuda grass straw	0.5	Revoke	No registered uses.
Cattle, fat	0.05	Revoke	180.6(a)(3)
Cattle, meat	0.05		
Cattle, meat byproducts	0.05		
Coffee beans	0.02	0.02	[Coffee, beans, green]
Corn grain	0.1	0.05	Residues from registered uses do not exceed 0.05 ppm for Codex harmonization. [Corn, field, grain]
Corn forage	0.5	0.5	[Corn, field, forage] [Corn, sweet, forage]
Cottonseed	0.05	0.05	[Cotton, undelinted seed]
Eggs	0.05	Revoke	180.6(a)(3)
Goats, fat	0.05	Revoke	180.6(a)(3)
Goats, meat	0.05		
Goats, meat byproducts	0.05		
Hogs, fat	0.05	Revoke	180.6(a)(3)
Hogs, meat	0.05		
Hogs, meat byproducts	0.05		
Hops	0.5	2	[Hops, cones, dried]

Table 4. Tolerance Reassessment Summary for Phorate.			
Commodity	Current Tolerance (ppm)	Tolerance Reassessment (ppm)	Comment/ [Correct Commodity Definition]
Horses, fat	0.05	Revoke	180.6(a)(3)
Horses, meat	0.05		
Horses, meat byproducts	0.05		
Lettuce	0.1	Revoke	No registered uses.
Milk	0.02	Revoke	180.6(a)(3)
Peanut vines	0.3	Revoke	Not considered a significant feed item (Table 1, 860.1000).
Peanut hay	0.3	Revoke	Feeding restriction exists.
Peanuts	0.1	0.1	
Potatoes	0.5	0.2	Residues from the registered uses do not exceed 0.2 ppm for Codex harmonization.
Poultry, fat	0.05	Revoke	180.6(a)(3)
Poultry, meat	0.05		
Poultry, meat byproducts	0.05		
Rice	0.1	Revoke	No registered uses.
Sheep, fat	0.05	Revoke	180.6(a)(3)
Sheep, meat	0.05		
Sheep, meat byproducts	0.05		
Sorghum fodder	0.1	0.1	[Sorghum, fodder]
Sorghum grain	0.1	0.05	Residues from the registered uses do not exceed 0.05 ppm for Codex harmonization. [Sorghum, grain]
Soybeans	0.1	0.05	Residues from registered uses do not exceed 0.05 ppm for Codex harmonization.
Sugar beet roots	0.3	0.3	[Sugar beets, roots]
Sugar beet tops	3	3	[Sugar beets, tops]
Sugarcane	0.1	0.05	Residues from the registered uses do not exceed 0.05 ppm.
Sweet corn (K+CWHR)	0.1	0.05	Residues from the registered uses do not exceed 0.05 ppm. [Corn, sweet (K+CWHR)]
Tomatoes	0.1	Revoke	No registered uses.

Table 4. Tolerance Reassessment Summary for Phorate.			
Commodity	Current Tolerance (ppm)	Tolerance Reassessment (ppm)	Comment/ [Correct Commodity Definition]
Wheat grain	0.05	0.05	[Wheat, grain]
Wheat (green fodder)	1.5	1.5	[Wheat, forage]
Wheat straw	0.05	0.05	[Wheat, straw]
Tolerances Listed Under 40 CFR §186.4750:			
Dried sugarbeet pulp	1	Revoke	Available data indicate that residues do not concentrate.
Tolerances to be Proposed:			
Corn, field, stover (fodder)	--	TBD ¹	
Corn, sweet, stover (fodder)	--	TBD	
Cotton, gin byproducts	--	TBD	
Sorghum, forage	--	TBD	
Wheat, hay	--	TBD	

¹ TBD = To be determined. Residue data are outstanding.

xiv. Codex Harmonization

The Codex Alimentarius Commission has established several maximum residue limits (MRLs) for phorate residues in various commodities (see *Guide to Codex Maximum Limits For Pesticide Residues, Part 2, FAO CX/PR, 4/91*). The Codex and U.S. tolerance expressions will be in harmony when the U.S. tolerance expression is revised to specify phorate, phorate sulfoxide, phorate sulfone, phorate oxygen analog, phorate oxygen analog sulfoxide, and phorate oxygen analog sulfone. A comparison of the Codex MRLs and the corresponding **reassessed** U.S. tolerances is presented in Table 5.

The following conclusions can be made regarding efforts to harmonize the U.S. tolerances with the Codex MRLs with respect to MRL/tolerance level: (i) compatibility between the U.S. tolerances and Codex MRLs exists for beans, cottonseed, eggs, field corn grain (maize), potatoes, sorghum, soybeans, and wheat; and (ii) incompatibility of the U.S. tolerances and Codex MRLs remains for field corn forage, peanuts, and sugar beet roots and tops because of differences in agricultural practices; no questions of compatibility exist with respect to commodities where Codex MRLs have been established but U.S. tolerances do not exist or will be revoked.

Table 5. Codex MRLs and applicable U.S. tolerances. Recommendations for compatibility are based on conclusions following reassessment of U.S. tolerances (see Table 4).				
Codex			Reassessed U.S. Tolerance (ppm)	Recommendation And Comments
Commodity (As Defined)	MRL ¹ (mg/kg)	Step		
Barley	0.05	CXL	Revoke	No registered uses in U.S.
Carrot	0.2 ²	7B	--	No registered uses in U.S.
Common bean (pods and/or immature seeds)	0.1	CXL	0.05	
Cotton seed	0.05	CXL	0.05	Compatibility exists.
Eggs	0.05 *	CXL	Revoke	
Beet fodder	0.05	CXL	--	No registered uses in U.S.
Maize	0.05	6	0.05	Compatibility exists.
Maize fodder	0.2	8	TBD ³	
Maize forage	0.1	5	0.5	
Meat	0.05 *	CXL	Revoke	
Milk	0.05 *	8	Revoke	
Peanut	0.05	7B	0.1	
Peanut oil, crude	0.05 *	5	--	
Peanut oil, edible	0.05 *	5	--	
Potato	0.2	7B	0.2	Compatibility exists.
Rape seed	0.1	CXL	--	No registered uses in U.S.
Sorghum	0.05	CXL	0.05	Compatibility exists.
Soya bean (dry)	0.05	CXL	0.05	Compatibility exists.
Sugar beet	0.05	8	0.3	
Sugar beet leaves or tops	1	8	3	
Tomato	0.1	CXL	Revoke	No registered uses in U.S.
Wheat	0.05	CXL	0.05	Compatibility exists.

¹ An asterisk (*) signifies that the MRL was established at or about the limit of detection.

² Decreased from 0.5 ppm by 1993 JMPR.

³ TBD = To be determined. Residue data are outstanding.

b. Dietary Exposure (Drinking Water Source)

A drinking water health advisory level for phorate and/or the phorate metabolites has not been established. Hydrolysis and microbial degradation appear to be the most important means of phorate dissipation in the environment. Phorate is very unstable to photolysis in water, but photolysis in the field may not be important since phorate

degrades rapidly by hydrolysis and aerobic soil metabolism. Also, phorate is incorporated or knifed in to a depth where sunlight does not contribute to its degradation. Phorate rapidly photolyses in water to form formaldehyde and phorate sulfoxide.

Parent phorate degrades in water with half-lives of 3 days at pH's 5, 7, and 9. Parent phorate is very mobile to essentially immobile in soil (Freundlich K_{ads} values of 1.5-20) depending on the soil organic carbon content, but is not persistent in aerobic soil ($T_{1/2}$ =3 days). In soil, parent phorate degrades into the oxidized metabolites phorate sulfoxide and sulfone. These metabolites are more persistent ($T_{1/2}$'s of 65 and 137 days, respectively) than parent phorate and more mobile, based on a laboratory soil column leaching study and a terrestrial field dissipation study that demonstrated significant mobility in soil. These metabolites are more likely to be present in water resources than parent phorate because they are more persistent and mobile.

i. Groundwater

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

Results from the SCI-GROW screening model predict that the maximum acute and chronic concentrations of total toxic residues (parent + sulfoxide+ sulfone) in shallow groundwater is not expected to exceed 13.5 $\mu\text{g/L}$ for the labeled use sites at the highest rate (4.5 lbs ai/A). The estimated concentrations in groundwater will be proportionally lower in relation to the amount applied because of the linear relationship between application rates and SCI-GROW Estimated Environmental Concentrations (EECs).

EPA's "Pesticides in Groundwater Database" reports no detections in 3,341 samples that have been submitted to date for parent phorate. This is consistent with the results of the laboratory and field dissipation studies, in which no downward mobility in soil of parent phorate was observed. Also, the metabolites phorate sulfoxide and sulfone were not detected in 12 samples, as reported in the Pesticides in Groundwater Database. However, the 12 samples reported do not represent a statistically-significant body of data. The environmental fate data indicate that the metabolites would likely be detected in shallow groundwater underlying permeable soils if more extensive sampling were conducted. Phorate sulfoxide and sulfone were detected to 12-18

inches of depth in a terrestrial field dissipation study in Georgia with permeable soils and normal rainfall.

ii. Surface Water

Environmental Fate and Effects Division (EFED) has estimated the concentration of phorate alone, and phorate plus degradates in surface water using the model PRZM/EXAMS. The estimated maximum peak concentration of phorate and degradates is 27.6 $\mu\text{g/L}$, and the maximum annual mean is 1.6 $\mu\text{g/L}$ (Breithaupt, 8/99). This model was not designed to estimate the levels in drinking water from a particular watershed, but can be used as a screening tool to identify pesticides which may have potential dietary risk concerns. For example, the PRZM model simulates a farm pond, and does not account for dilution, water treatment, movement (rivers, creeks), or turnover (reservoirs).

Monitoring studies have been conducted for phorate only in the Mississippi Basin, Illinois, Colorado, and Florida. Analyses from an IL study were reported as total phorate + sulfoxide + sulfone. No monitoring data are available for the metabolites. Only two detects were noted for the Colorado agricultural watershed (out of 25) at concentrations ranging from 0.08 $\mu\text{g/L}$ to 0.6 $\mu\text{g/L}$. Phorate was not detected in any of the other samples from any of the other studies. The monitoring data are likely to be of little utility for dietary risk assessment, since the oxidized metabolites are more likely to be present than the parent, but in almost all of the studies, analyses for the metabolites were not conducted.

c. Dietary Risk Assessment and Characterization

i. Chronic Dietary Risk from Food Sources

A chronic dietary analysis was conducted using a chronic Population Adjusted Dose (cPAD) of 0.0002 mg/kg body weight/day (refer to section 2.b. for discussion of endpoint). The chronic dietary analysis was conducted using percent crop treated values, anticipated residues, processing factors and recommendations for tolerance reassessments. A summary of considerations used in the chronic analysis is included in Table 7 on page 31. Results of these analyses for selected population subgroups are presented in Table 6.

Table 6. Results of Chronic Dietary Risk Analysis for Phorate

Population Subgroup	Exposure (mg/kg/day)	%cPAD ¹
General U'S Population	0.000006	3.5
All Infants (<1 year)	0.000002	1.4
Nursing Infants (<1 year)	0.000001	0.5
Non-Nursing Infants (<1 year)	0.000003	1.8
Children (1-6 years)	0.000014	8.5
Children (6-12 years)	0.000010	5.9
Females (13-50 years)	0.000004	2.6
Males (20+ years)	0.000005	2.8

¹ %PAD = Percent Population Adjusted Dose consumed (PAD = RfD/FQPA Safety Factor).

Drinking water was not included in this dietary risk analysis. When the recommendations for reassessed tolerances are considered in the risk analysis, including revocation of all meat and milk tolerances, then the chronic dietary risk from food sources only, is below our level of concern. The Food Quality Protection Act requires re-evaluation of percent crop treated values and anticipated residue values every five years whenever they are used in a dietary risk assessment.

ii. Acute Dietary Risk from Food Sources

The acute dietary toxicological endpoint of concern is miosis observed in an acute rat neurotoxicity study (refer to section 2f.i. for a discussion of the acute dietary endpoint). The Agency has conducted several acute dietary risk analyses using DEEM™ software, which uses Monte Carlo simulations to estimate the percent of the acute population adjusted dose (aPAD) consumed by multiple subpopulations (Swartz, 2/18/99). The analysis used food consumption data from the 1989-1992 USDA CSFII survey, information on the percent of crop treated (Alsadek, 1/18/98), and data from field trial studies. A summary of the assumptions used, residue values, processing factors, and use patterns on which the dietary analyses are based, is presented in Table 7. No processed sugar commodity residues were used in the analysis since residues are destroyed by the lime and carbonation process. The results of the Agency analyses are presented in Table 8. Some of the analyses exclude individual commodities in order to determine which commodities significantly contribute to the risk. The registrant has submitted two acute dietary risk analyses which have been found deficient for various reasons (Miller, 1998; Olinger, 1999).

Based on inclusion of commodities supported in reregistration, acute dietary risk for phorate is below the Agency's level of concern for the general US population and all population subgroups, including infants and children. The most highly exposed subgroup is children 1-6, with 68% of the aPAD consumed. Selective exclusion of various commodities from the analysis indicates that peanuts, potatoes, and sweet corn contribute most significantly to acute dietary risk for phorate. Greater risk reduction for children 1-6 was achieved by excluding sweet corn than by excluding peanuts or potatoes. Exclusion of potatoes, sweet corn and peanuts together significantly reduced the acute dietary risk for all population subgroups.

Monitoring data are available from Food and Drug Administration (FDA) and the U.S. Department of Agriculture (USDA) Pesticide Data Program (PDP), but were not used in the quantitative risk assessment. FDA is responsible for enforcing pesticide tolerances and routinely analyzes for the parent compound and the regulated metabolites. The PDP has analyzed raw agricultural commodities for residues of phorate for several years, and more recently has included several (but not all) of the metabolites as well. Neither FDA nor PDP has found residues exceeding the limit of quantitation in any commodity since 1993 with the exception of potatoes. Even for potatoes, the rate of detections is low (<2%), and no samples have exceeded the existing tolerance. Several samples within the past few years had residues close to the recommended tolerance reassessment of 0.2 ppm, indicating there is a slight potential for residues close to the tolerance on the raw commodity. Consumer practices, cooking, and processing studies generally show that residues in potatoes are significantly reduced when potatoes undergo typical cooking and preparation procedures.

Field trial data were used in the quantitative risk assessment because the data provided the highest level of refinement. The limits of detection for all phorate residues were lower in the field trial studies than the combined limits of detection found in the FDA monitoring data.

Table 7. Summary of Considerations Used in the Acute and Chronic Dietary Risk Analyses

Crop	Recommended Tolerance Reassessment, ppm	Acute Anticipated Residue Value, ppm ¹	Chronic Anticipated Residue Value, ppm	Percent Crop Treated	Processing Factors	Maximum Use Pattern Considered on Which the Dietary Exposure Assessment is based	Comments
Beans, dry	0.05	0.00075	0.00075	3	None	2.04 lb ai/A at planting	Used %CT x ½ LOQ. Insufficient information was available to determine LODs. Blended commodity, so a point estimate was used.
Beans, succulent	0.05	0.025, distribution	0.001	4	None	2.04 lb ai/A at planting, PHI = 60 days	All samples non-detect, so used ½ LOQ = 0.025 ppm for all "treated" samples in the distribution. Insufficient information was available to determine LODs. Chronic AR = 0.025 x %CT. Zero residues were assumed for all untreated samples.
Coffee	0.02	0.0006	0.0006	3	0.06 Roasting	(Not a U.S. use) 1 g ai/plant/year of plant life	Used tolerance x %CT. Insufficient information was available to determine LODs. Blended commodity, so a point estimate was used. Residues were non-detectable in the field trial studies.
Corn, Field	0.05	0.00005	0.00005	1	refined oil 0.81	1.3 lb ai/A at planting and at cultivation PHI = 30 days	Used %CT x ½ LOQ. Insufficient information was available to confirm the LODs. Blended commodity, so a point estimate was used. Residues were non-detectable in the field trial studies.
Corn, Sweet	0.05	0.05, distribution	0.01	20	None	1.3 lb ai/A at planting and at cultivation PHI = 30 days	Only four valid field trials, all detects - used proposed tolerance reassessment value for each detect due to the lack of data.

Table 7 continued from previous page

Crop	Recommended Tolerance Reassessment, ppm	Acute Anticipated Residue Value, ppm ¹	Chronic Anticipated Residue Value, ppm	Percent Crop Treated	Processing Factors	Maximum Use Pattern Considered on Which the Dietary Exposure Assessment is based	Comments
Cotton	0.05	0.0015	0.0015	6	None	1.64 lb ai/A at planting + 2.18 lb ai/A side dress PHI = 60 days.	All field trials non-detect. Used %CT x ½ LOQ. Insufficient information was available to determine LODs. Blended commodity, so a point estimate was used.
Peanuts	0.1	0.006	0.006	12	None	1.5 lb ai/A at planting; 3 lb ai/A at pegging. PHI = 90 days. Only one pegging treatment per season.	Used average of three field trials x the %CT. Residues were detected in all three field trials, reflecting PHIs from 70-90 days. Most 90-day PHI data reflected exaggerated rates and showed residues exceeding the proposed tolerance reassessment. Blended commodity, so a point estimate was used.
Potatoes	0.2	Distribution, 0.002 - 0.15	0.001	24	0.46 cooked 0.49 fried 0.46 boiled 0.26 peeled 0.44 peeled & cooked 0.27 peeled & boiled 1.2 dry	2.4-3.5 lb ai/A at planting or 2.3 lb ai/A post-emergence. PHI = 90 days	Thirteen field trials are available, four detects, and nine non-detects; used some ½ LOD and some ½ LOQ for non-detects. Chronic estimate = %CT x average residue value.
Grain Sorghum	0.05	0.00025	0.00025	1	None	1.3 lb ai/A at planting + 2 nd application at cultivation. PHI = 30 days	Used %CT x ½ LOQ. Insufficient information was available to determine LODs. Residues were non-detectable in all field trials. Blended commodity, so a point estimate was used.

Crop	Recommended Tolerance Reassessment, ppm	Acute Anticipated Residue Value, ppm ¹	Chronic Anticipated Residue Value, ppm	Percent Crop Treated	Processing Factors	Maximum Use Pattern Considered on Which the Dietary Exposure Assessment is based	Comments
Soybeans	0.05	0.00005	0.00005	1	None	1.96 lb ai/A	Used %CT x ½ LOD. EPA estimate of LOD is 0.01. Residues were non-detectable in all field trials. Blended commodity, so a point estimate was used.
Wheat	0.05	0.00015	0.00015	1	None	0.98 lb ai/A at planting. PHI = 70 days.	Used %CT x average of six field trials, three at ½ LOQ, and three at ½ the highest LOD. Residues were non-detectable in all field trials. Blended commodity, so a point estimate was used.

¹ Point estimates were used for "blended" commodities. Distributions of residue values were used for "non-blended" commodities.

Table 8. Results of Acute Dietary Exposure/Risk Analyses for Phorate¹
[Based on the 99.9th Percentile of Exposure]

	All Commodities		All Commodities, Excluding Potatoes		All Commodities, Excluding Sweet Corn		All Commodities Excluding Peanuts		Excluding Potatoes, Sweet Corn and Peanuts		Including Only Potatoes, Sweet Corn and Peanuts	
Population Subgroup	Exposure (mg/kg/day)	%aPAD	Exposure (mg/kg/day)	%aPAD	Exposure (mg/kg/day)	%aPAD	Exposure (mg/kg/day)	%aPAD	Exposure (mg/kg/day)	%aPAD	Exposure (mg/kg/day)	%aPAD
US Population	0.000317	38	0.000264	32	0.000223	27	0.000314	38	0.000050	6.1	0.000318	38
Infants	0.000318	38	0.000270	32	0.000225	27	0.000321	38	0.000151	18	0.000315	38
Nursing Infants	0.000145	17	0.000007	0.8	0.000115	14	0.000161	17	0.000001	0.2	0.000147	18
Non-Nursing Infants	0.000355	43	0.000272	33	0.000236	28	0.000343	41	0.000194	23	0.000398	48
Children 1-6	0.000561	68	0.000533	64	0.000382	46	0.000572	68	0.000107	13	0.000563	68
Children 7-12	0.000374	45	0.000293	35	0.000309	37	0.000377	45	0.000060	7.2	0.000390	47
Females 13-50	0.000225	27	0.000197	24	0.000163	20	0.000225	27	0.000041	4.9	0.000228	27
Males 20+	0.000220	26	0.000168	20	0.000172	21	0.000219	26	0.000039	4.8	0.000223	27

¹ Exposure is presented in mg/kg/day, at the 99.9th percentile of exposure. The %aPAD is the % of the acute Population Adjusted Dose consumed.

iii. Drinking Water Risk (Acute and Chronic)

Drinking water levels of comparison (DWLOCs) for acute and chronic exposure to phorate in surface and groundwater and are presented in Tables 9a and 9b. The $DWLOC_{acute}$ is the concentration in drinking water as a part of the aggregate acute exposure that occupies no more than 100% of the acute PAD. To calculate the DWLOC for acute exposure relative to an acute toxicity endpoint, the acute dietary food exposure (from the DEEM analysis) was subtracted from the acute PAD. The $DWLOC_{chronic}$ is the concentration in drinking water as a part of the aggregate chronic exposure that occupies no more than 100% of the chronic PAD. To calculate the DWLOC for chronic (non-cancer) exposure relative to a chronic toxicity endpoint, the chronic dietary food exposure (from DEEM) was subtracted from the chronic PAD to obtain the acceptable chronic (non-cancer) exposure to phorate in drinking water. DWLOCs were then calculated using default body weights and drinking water consumption figures.

The estimated maximum concentrations of phorate and metabolites of concern in groundwater is $13.5 \mu\text{g/L}$; for the purposes of the screening-level assessment, the maximum and average concentrations in groundwater are not believed to vary significantly. The estimated peak concentration of phorate and metabolites of concern in surface water is $27.6 \mu\text{g/L}$, and the annual mean is $1.6 \mu\text{g/L}$. [The maximum estimated concentrations of phorate and metabolites in groundwater are greater than HED's levels of comparison (DWLOC) for phorate in drinking water as a contribution to chronic aggregate exposure.] The estimated surface water concentrations are less than or equal to the DWLOCs for chronic and acute risk. At this time HED can make no conclusions regarding the risk from exposure to phorate and its metabolites in drinking water.

Table 9a. DWLOCs for Chronic Exposure to Phorate and Metabolites

Population Subgroup	Chronic Scenario						
	Chronic PAD (mg/kg/day)	Food Exposure (mg/kg/day)	Maximum Water Exposure (mg/kg/day)	SCI-GROW (All residues, $\mu\text{g/L}$)	PRZM/EXAMS (Parent Only, $\mu\text{g/L}$)	PRZM/EXAMS (All residues, $\mu\text{g/L}$)	DWLOC (CHRONIC) ($\mu\text{g/L}$)
U.S. Population	1.70e-04	6.00e-06	1.64e-04	13.5	0.2	1.6	5.7
Females 13+	1.70e-04	5.00e-06	1.65e-04	13.5	0.2	1.6	5.0
Children 1-6	1.70e-04	1.50e-05	1.55e-04	13.5	0.2	1.6	1.6

Table 9b. DWLOCs for Acute Exposure to Phorate and Metabolites

Population Subgroup	Acute Scenario						
	Acute PAD (mg/kg/day)	Food Exposure (mg/kg/day)	Maximum Water Exposure (mg/kg/day)	SCI-GROW (All residues, $\mu\text{g/L}$)	PRZM/EXAMS (Parent Only, $\mu\text{g/L}$)	PRZM/EXAMS (All residues, $\mu\text{g/L}$)	DWLOC (Acute) ($\mu\text{g/L}$)
U.S. Population	8.30e-04	3.17e-04	5.13e-04	13.5	23.1	27.9	18.0
Females 13+	8.30e-04	2.25e-04	6.05e-04	13.5	23.1	27.9	18.0
Children 1-6	8.30e-04	5.64e-04	2.66e-04	13.5	23.1	27.9	2.7

4. Occupational and Residential Exposure and Risk Characterization

a. Occupational and Residential Exposure

An occupational exposure assessment has been conducted for handlers (mixers, loaders, applicators, etc.) during use or to persons entering treated sites after application is complete.

i. Summary of Use Patterns and Formulations: Occupational and Residential

Phorate is an organophosphate insecticide and nematicide formulated as a granular (6.5 to 20 percent ai) and as an emulsifiable concentrate manufacturing product (92 to 95 percent ai). There are no current registrations for greenhouse or indoor uses of phorate, but currently there are two 24(c) registration for application at-planting to field-grown lilies and daffodils.

Phorate can be applied by aircraft and ground equipment (soil band treatment, soil in-furrow treatment, soil drill treatment, soil side dress treatment) to beans, corn, cotton, daffodils, lilies, peanuts, potatoes, sorghum, soybeans, sugar beets, sugarcane, sweet corn, and wheat. The maximum application rates range from 1.3 to 3.9 lb ai/acre (and 8 lb ai/A for bulbs only). Only one application per season is allowed for most of the uses. Two applications per season are allowed for irrigated cotton, sorghum, peanuts, and sugar beets. The interval between applications ranges from 1 to 2 months.

At this time products containing phorate are intended primarily for occupational uses and not for homeowner uses; therefore, no residential exposures are expected.

ii. Mixer/Loader/Applicator Exposure Assessment

The tasks associated with phorate use (i.e., for "handlers") that could lead to occupational exposure can generally be categorized using the following terms:

- Occupational Mixer/loaders: these individuals perform tasks in preparation for an application. For example, they would load/transfer solid materials (e.g., granulars such as Thimet 20G) into application equipment such as a planter prior to application.
- Occupational Applicators: these individuals operate application equipment during the release of a pesticide product. These individuals can make applications using equipment such as tractor-drawn spreaders and planters for granular materials.

- Occupational flaggers: these individuals guide aircraft to appropriate locations during the aerial release of pesticide products.
- Occupational Mixer/loader/applicators: these individuals are involved in the entire pesticide application process (i.e., they do all job functions related to a pesticide application event). These individuals would load a granular into a planter and then also complete an application. There are growers who would complete all aspects of an application event. As such, risks have been calculated for these individuals.

The Agency classifies these occupational exposure scenarios as short-term exposures (one-week or less) and intermediate-term exposures (seven days to several months). Although phorate is applied mostly once per season, some applicators may apply phorate over a period up to 12 weeks because they need to cover large acreage or they may be custom or professional applicators. Typically the Agency conducts separate assessments for exposures less than one week, and greater than one week, for pesticides with the use patterns previously described. The toxicity information for phorate also indicates that the Agency needs to separately consider exposures to the skin and exposures via inhalation because of different dose levels in the studies selected for dermal and inhalation risk assessments.

Generally, the Agency prefers to use chemical- and scenario-specific data to assess occupational exposures. In the absence of these data, the Agency uses monitoring data from similar exposure scenarios that have been collected and incorporated into a system known as the Pesticide Handlers Exposure Database (PHED). In the case of phorate, the registrant submitted an exposure study for a similar chemical, terbufos (1999, MRID 44800701). Exposure data from this study reflected use of a closed loading system and varying levels of personal protection. PHED data were used for all scenarios for which chemical-specific data were not available.

PHED, a library of actual exposure monitoring data that can be used to analyze specific types of exposures for those individuals involved in the application of pesticides (e.g., mixer/loaders, applicators), was used for many of the quantitative risk assessments that were completed for phorate. This system has been in use worldwide since 1992 and was developed by a task force that includes the EPA, Health Canada, the California Department of Pesticide Regulation, and the pesticide industry. The scientific basis for PHED has long been accepted by these groups. PHED forms the backbone of the vast majority of handler risk assessments completed by the Agency. The system now contains data from approximately 1700 exposures which were monitored when individuals were making actual pesticide applications in a variety of settings.

To add consistency to the values produced from this system and to ensure quality control, the PHED Task Force has evaluated all data within the system and has developed a set of grading criteria to characterize the quality of the original study data. The assessment of data quality is based on the number of observations and the

available quality control data. The data used in this assessment were generally of low quality, the exception being the data reflecting the use of engineering controls.

The basis of PHED is that individual handler exposures are related to how an application is made and not the specific pesticide being applied. The aspects of an application that are thought to affect exposures include: the kinds of equipment involved in application; the nature of the product being used (e.g., formulation and packaging); the application parameters such as application rate and total pounds of active ingredient applied; and the devices used by an individual to protect themselves during an application (e.g., additional clothing, chemical-resistant gloves, and closed tractor cabs).

The values that are calculated using PHED are called unit exposures and are generally presented as milligrams (or 1/1000th of a gram) exposure of active ingredient per pound active ingredient applied. For example, if one makes similar groundboom applications of 10 pounds of pesticide A or B, the unit exposures (1/10th of the exposure from applying 10 pounds of active ingredient A or B) would be proportional to the total amount applied and not whether pesticide A or B was in the spray tank. Separate unit exposures are typically calculated for the different equipment types that can be used in applications (e.g., open-cab groundboom and airblast applications would have different unit exposures). Separate unit exposures are also calculated for varying protective measures used during application with the same equipment. For example, there are specific unit exposures for groundboom applications for individuals wearing normal work clothing, wearing normal work clothing under coveralls and with gloves, and for making applications using a closed cab tractor. In cases where data are not complete, the Agency uses available data and standard measures of protection to estimate exposure levels. For example, the Agency believes that the use of a coverall or a pair of chemical-resistant gloves provide a certain amount of protection. These levels of protection and similar exposure data are used to calculate exposures where directly applicable data are not complete.

Along with the exposure values considered in the risk assessment (obtained from PHED), other information is needed to calculate the risk. Values needed are application rates, number of acres treated per day, body weight, and frequency of application. Amount of active ingredient handled per day is based on the number of acres treated and the application rate. These values are coupled with the unit exposures to calculate the daily exposure to the worker.

Initially the Agency calculates the risk using the least amount of protective measures, which is called the baseline assessment. For those involved in applications this usually represents an individual's normal work clothing, i.e. long sleeve shirts, long pants, no gloves, and no respirator. If there is a concern at this level, the Agency would require the use of devices to lower the risk. The first kinds of devices we would require are referred to as personal protective equipment (PPE), which can include an extra layer of clothing, chemical-resistant gloves, and respirators. If concerns persist, then the

Agency would require additional protective measures often described as engineering controls. Common examples of engineering controls include enclosed tractor cabs, closed loading systems, and gel packs. This approach is commonly referred to as a tiered approach, and is well established in the area of risk assessment.

Product labels generally specify a certain level of PPE. However because the labels for older products are generally not based on a risk assessment, the Agency must begin its assessment assuming baseline measures and increase those measures until an acceptable level is obtained. Therefore any proposed label modifications will be based on this risk assessment instead of standard label recommendations.

In addition to PHED, the application rate and daily amount treated (usually acres per day) are also key elements in the calculation of handler exposures because they are used in the calculation of the amount used to complete applications on a daily basis. A range of application rates derived from phorate labeling, data from the registrant, and the data from the latest Quantitative Usage Analysis serve as the basis for this assessment. A summary of assumptions with regard to acres treated per day, application rates, and amount active ingredient handled may be found in Table 10.

Dermal and inhalation unit exposures from PHED or chemical specific data are combined with application rates and amount of acres treated per day to calculate the daily doses in mg/kg/day. The doses calculated for peanuts, the crop leading to the highest daily exposure, are presented in Table 11. The daily doses for other crops are proportionally lower, depending upon the amount handled per day.

Table 10. Summary of Application Assumptions			
Crop	Application Rate, lb ai/A	Acres Treated per Day	Amount a.i. Handled per Day
Beans	2	80	160
Corn	1.3	213	277
Cotton	2.2	80	176
Lilies and Daffodils	8	40	320
Peanuts	3	120 ¹	360
Potatoes	3.5	100	350
Sorghum	1.3	130 ¹	169
Soybeans	2	150 ¹	300
Sugar Beets	1.5	130	195
Sugarcane	3.9	80 ¹	320
Wheat	1.0	200	200

¹ Value defined by registrant; different from Agency defaults.

iii. Post-Application Exposure Assessment

Two soil residue dissipation studies conducted in peanuts and potatoes were available that indicated phorate residues persist for many weeks after application. Post-application exposure to phorate residues could occur if there were activities which would involve significant disturbance of soil, followed by prolonged contact with the soil. Additional information regarding cultural practices would allow the Agency to determine whether a quantitative risk assessment is feasible. At this time insufficient reliable information is available to complete such an assessment.

Table 11. Summary of Daily Occupational Exposures for Application to Peanuts ¹			
Scenario	Exposure Data Source	Daily Dermal Dose mg/kg/day	Daily Inhalation Dose mg/kg/day
Loaders			
Loading Clay Based Granules - BASELINE ⁵	PHED	4.32×10^{-2}	8.74×10^{-3}
Loading Clay Based Granules - Minimum PPE ⁷	PHED	3.55×10^{-2}	1.75×10^{-3}
Loading Clay Based Granules - Maximum PPE ⁸	PHED	1.75×10^{-2}	8.74×10^{-4}
Loading Clay Based Granules for aerial application - Closed Loading System	PHED	8.64×10^{-4}	1.75×10^{-4}
Loading Clay Based Granules - Closed Loading System, Apron, Gloves, No Respirator	MRID 44800701 ²	2.67×10^{-4}	3.1×10^{-5}
Loading Clay Based Granules - Closed Loading System, Apron, Gloves, PF 10 Respirator	MRID 44800701 ²	2.67×10^{-4}	3.1×10^{-6}
Applicators			
Applying Granular formulations with Ground-based Equipment - BASELINE ⁵	PHED	5.09×10^{-2}	6.17×10^{-3}
Applying Granular formulations with Ground-based Equipment - Minimum PPE ⁷	PHED	3.70×10^{-2}	1.23×10^{-3}
Applying Granular formulations with Ground-based Equipment - Maximum PPE ⁸	PHED	2.16×10^{-2}	6.17×10^{-4}
Applying Granular formulations with Ground-based Equipment - Enclosed Cab	PHED	1.08×10^{-2}	1.13×10^{-3}
Applying Granular formulations with Aerial Equipment - Enclosed Cab	PHED	8.74×10^{-3}	6.69×10^{-3}
Applying Granular formulations with Ground-based Equipment - Open Cab , Apron, Gloves, No Respirator	MRID 44800701 ²	1.81×10^{-4}	1.25×10^{-5}
Applying Granular formulations with Ground-based Equipment - Open Cab , Apron, Gloves, PF 10 Respirator	MRID 44800701 ²	1.81×10^{-4}	1.25×10^{-6}

Table 11. Summary of Daily Occupational Exposures for Application to Peanuts ¹			
Scenario	Exposure Data Source	Daily Dermal Dose mg/kg/day	Daily Inhalation Dose mg/kg/day
Combined Loader and Applicator			
Loading and Applying Granular formulations with Ground-based Equipment - Closed Loading System, Open Cab, Apron, Gloves, No Respirator	MRID 44800701 ²	4.48×10^{-4}	3.35×10^{-5}
Applying Granular formulations with Ground-based Equipment - Open Cab, Apron, Gloves, PF10 Respirator	MRID 44800701 ²	4.48×10^{-4}	3.35×10^{-6}
Flaggers			
Flagging for Aerial Spray Operations - BASELINE ⁶	PHED	1.44×10^{-2}	7.71×10^{-4}
Flagging for Aerial Spray Operations - Minimum PPE ⁷	PHED	1.39×10^{-2}	1.54×10^{-4}
Flagging for Aerial Spray Operations - Maximum PPE ⁸	PHED	8.23×10^{-3}	7.71×10^{-5}
Flagging for Aerial Spray Operations - Engineering controls	PHED	2.88×10^{-4}	1.54×10^{-5}

¹ Only the doses for peanuts are shown since application to peanuts leads to the highest daily exposure of any crop.

² Data from the study are geometric means.

b. Occupational and Residential Risk Assessment/Characterization

i. Risk from Dermal and Inhalation Exposure

Toxicity endpoints to be used in the occupational risk assessment are discussed in Section B.2.f and Table 2 of this document. Two dermal endpoints were selected, one for exposures less than 28 days, and one for greater than 28 days. Inhalation endpoints were selected for exposures of seven days or less, and greater than seven days. The registrant has estimated maximum exposure intervals of six to eight weeks. Because of the varying intervals of exposure for the dermal and inhalation endpoints, risk estimates were determined for the following three exposure intervals: 1) seven days or less; 2) 8 to 28 days; and 3) greater than 28 days.

A comprehensive presentation of the calculation of the risk estimates may be found in the most recent Occupational Exposure and Risk Assessment (Dawson, 1999). A summary of the ranges of combined dermal and inhalation Margins of Exposure (MOEs) for all crops may be found in Table 12. Generally the Agency is not concerned when the MOE exceeds 100. Scenarios for which the MOE is greater than 100 for all exposure durations are highlighted in Table 12.

ii. Incident Reports

In addition to use of margins of exposure to estimate the risk, incident data are considered (Blondell, 1999). The following databases were consulted for poisoning incident data on the active ingredient phorate:

- OPP Incident Data System (IDS);
- Poison Control Centers - (data received in response to 1993 Data-Call-In covering the years 1985 to 1992);
- California of Pesticide Regulation ; and,
- National Pesticide Telecommunication Network (NPTN).

IDS (as of 8/99) received seven separate incident reports involving human exposure. Poison Control Centers Data (1985 to 1992) showed 109 cases of occupational and 82 cases of non-occupational exposure to phorate. Poison Control Centers data for the interval 1993-1996 showed a decrease in the rate of incidences, 33 cases of occupational and 27 cases of non-occupational exposure. California data (1982-1993) showed 22 cases of adverse reactions to phorate. NPTN (1985-1991) handled 116 calls on phorate involving 39 incidents (29 humans, 5 animals, and 5 other, e.g. plants, wildlife).

The risk from phorate exposure tended to be higher than other cholinesterase inhibitors. Of the 28 insecticides with Poison Control Center data (1985-1992), phorate

ranked 6 for occupational exposure and 7 for non-occupational exposure, with number 1 being most frequently associated with adverse effects. This suggests that phorate is above average in its ability to cause adverse effects.

When using the California data and calculating ratios for the number of systemic poisonings per 1,000 applications, the calculations for phorate are higher than the median score for the 28 other insecticides. Note, however, that California calculations were based on a relatively small number of cases. Applicators and mixer/loaders are the most frequently affected activity categories.

Phorate is currently only used in granular formulations. Some of the above average ratios or measures of hazard (described above) suggest that handlers may not fully observe precautions because of the perception that poisoning is much less likely with a granular than liquid formulation.

iii. Occupational Risk Characterization

The scenario-specific study has been used by the Agency to assess the exposures of individuals using phorate in "Lock-N-Load" or closed system packaging with closed cab application (i.e., "Lock-N-Load" is about 65 percent of the phorate market). When the geometric mean values from the scenario-specific exposure studies serve as the basis of the assessment, the Agency has no concerns over the use of phorate granular formulations in "Lock-N-Load" packaging and application with closed cabs (also given the same levels of personal protective equipment used in the study) for any exposure scenario (including all durations) considered in this assessment.

Packaging that can lead to open exposure scenarios (e.g., bags that are torn open where the user can come into direct contact with the chemical) accounts for the remaining 35 percent of the phorate market. These exposures were assessed using data from the PHED and not using the study referenced above for "Lock-N-Load" packaging/closed-cab applications and back-calculating exposure values using a protection factor as was done in the risk assessment submitted by the registrant. The PHED data used in the assessment are more appropriate than the approach used in the registrant submitted risk assessment in which a generic protection factor was used to back calculate exposures. [Note: Another exposure study was conducted for terbufos using a 20CR formulation and open loading/open cab applications. The Agency did not bridge these data for phorate and instead used PHED. This is also the same approach taken in the registrant submitted risk assessment -- no bridging was completed using the 20CR data.] The analysis completed using PHED indicates that the Agency generally has no concerns for loaders if the exposure durations are <28 days and flaggers (aerial applications are allowed but not expected to be significant) at any duration if engineering controls are used. The Agency has concerns for ground-based

and aerial applicators at any exposure duration even if engineering controls are used (MOEs > 20 for durations up to 28 days and generally < 10 thereafter). In all cases, where the Agency has risk concerns, the predominant contributor (i.e., driver) to the overall or total risk appears to be the duration of exposure. Exposure scenarios with durations > 28 days have the most significant risks associated with them. The Agency fully anticipates that the duration of a majority of exposures will be less than 28 days and that the population who are exposed to phorate for greater than 28 days will be small.

The incident data are supportive of the Agency's risk estimates for individuals who may load and apply products containing phorate. Many of the occupational incidents involving phorate occurred when personal protective equipment was not used. The Agency's risk estimates exceeded the level of concern for those scenarios with minimal or no personal protective equipment.

Two soil residue dissipation studies conducted in peanuts and potatoes were available that indicated phorate residues persist for many weeks after application. The Agency did not complete a quantitative risk assessment for post-application exposures because additional information on cultural practices for crops, where soil contact resulting in occupational post-application scenarios is likely, are needed to determine if additional data are required. From a qualitative perspective, the residues appear to be potentially available for exposure. However, it is not clear if there are activities that involve significant disturbance of the soil which would contribute to exposure.

Table 12. Summary of Phorate Occupational Risk Estimates

Scenario	Exposure Data Source ¹	Range of Combined Dermal and Inhalation MOEs ²		
		≤ 7 days Exposure ³	8-28 days Exposure ⁴	>28 days Exposure ⁵
Loaders				
Loading Clay Based Granules - BASELINE ⁶	PHED	7-28	4-14	1- 4
Loading Clay Based Granules - Minimum PPE ⁷	PHED	11-43	8-33	11-43
Loading Clay Based Granules - Maximum PPE ⁸	PHED	22-86	17-66	3-11
Loading Clay Based Granules for aerial application - Closed Loading System	PHED	354-1419	178-714	48-193
Loading Clay Based Granules - Closed Loading System, Apron, Gloves, No Respirator	MRID 44800701 ⁹	1220-4895	682-2739	162-652
Loading Clay Based Granules - Closed Loading System, Apron, Gloves, PF 10 Respirator	MRID 44800701 ⁹	1482-5947	1353-5428	184-739
Applicators				
Applying Granular formulations with Ground-based Equipment - BASELINE ⁶	PHED	11-43	8-33	1-5
Applying Granular formulations with Ground-based Equipment - Minimum PPE ⁷	PHED	10 - 42	9 - 35	1 - 5
Applying Granular formulations with Ground-based Equipment - Maximum PPE ⁸	PHED	18-72	15-61	2-9

Table 12, continued

Scenario	Exposure Data Source ¹	Range of Combined Dermal and Inhalation MOEs ²		
		≤ 7 days Exposure ³	8-28 days Exposure ⁴	>28 days Exposure ⁵
Applying Granular formulations with Ground-based Equipment - Enclosed Cab, No PPE	PHED	32-129	20-82	4-17
Applying Granular formulations with Aerial Equipment - Enclosed Cab	PHED	21-83	6-26	3-13
Applying Granular formulations with Ground-based Equipment - Open Cab, Apron, Gloves, No Respirator	MRID 44800701 ⁹	2022-8114	1440-5778	259-1040
Applying Granular formulations with Ground-based Equipment - Open Cab, Apron, Gloves, PF 10 Respirator	MRID 44800701 ⁹	2224-8926	2129-8546	275-1104
Combined Loader and Applicator				
Loading and Applying Granular formulations with Ground-based Equipment - Closed Loading System, Open Cab, Apron, Gloves, No Respirator	MRID 44800701 ⁹	761-3053	463-1858	100-401
Applying Granular formulations with Ground-based Equipment - Open Cab, Apron, Gloves, PF10 Respirator	MRID 44800701 ⁹	889-3569	827-3320	110-443
Flaggers				
Flagging for Aerial Spray Operations - BASELINE ⁶	PHED	26-104	20-79	3-13
Flagging for Aerial Spray Operations - Minimum PPE ⁷	PHED	29-115	27-108	4-14

Table 12, continued

Scenario	Exposure Data Source ¹	Range of Combined Dermal and Inhalation MOEs ²		
		≤ 7 days Exposure ³	8-28 days Exposure ⁴	>28 days Exposure ⁵
Flagging for Aerial Spray Operations - Maximum PPE ⁶	PHED	49-195	46-184	6-24
Flagging for Aerial Spray Operations - Engineering controls	PHED	1297-5205	382-3943	165-661

¹ Study data are of acceptable quality; most PHED data were of low quality with the exception of engineering control data, which were high quality.

² A Margin of Exposure (MOE) of greater than 100 is considered to be protective. Scenarios for which the MOE exceeded 100 for all exposure durations are highlighted.

³ Based on a dermal NOAEL of 0.406 mg/kg/day and a inhalation NOAEL of 0.25 mg/kg/day.

⁴ Based on a dermal NOAEL of 0.406 mg/kg/day and a inhalation NOAEL of 0.05 mg/kg/day. Inhalation toxicity is assumed to be equivalent to oral toxicity, i.e. 100% dermal and inhalation absorption.

⁵ Based on a dermal NOAEL of 0.05 mg/kg/day and a inhalation NOAEL of 0.05 mg/kg/day. Dermal and inhalation toxicity is assumed to be equivalent to oral toxicity, i.e. 100% dermal and inhalation absorption.

⁶ Baseline assessment assumes typical work clothing with no added protection.

⁷ Minimum PPE assumes use of gloves and a dust/mist respirator with a protection factor of 5.

⁸ Maximum PPE assumes use of double layer of clothing, gloves, and an air purifying respirator with a protection factor of 10.

⁹ Geometric means are reported for all results from MRID 44800701.

013731

c. Statement of the Adequacy of the Residential Exposure Database to Assess Infant's and Children's Exposures

Phorate is only applied to agricultural crops or to field-grown nursery stock. Accordingly, the Agency has no residential exposure concerns for infants and children, and no data are required to assess such exposure.

5. Aggregate Exposure and Risk Assessment/Characterization

The Agency has no concerns for the general U.S. population, including infants and children, from residential exposure to phorate. Therefore only dietary exposures (food and water) to phorate need be considered in the aggregate assessments.

a. Acute Aggregate Exposure and Risk

The Agency does not have sufficient reliable data to quantitate the risk from water, but screening information which is available suggests that there is a potential acute dietary risk concern from water. The total dietary exposure from water and food sources cannot be combined at this time for a total dietary or aggregate risk. **The dietary risk from food sources alone is below the Agency's level of concern for acute risk.**

b. Chronic Aggregate Exposure and Risk

The Agency does not have sufficient reliable data to quantitate the risk from water, but screening information which is available suggests that there is a potential chronic dietary risk concern from water. The total dietary exposure from water and food sources cannot be combined for a total dietary or aggregate risk at this time. **The dietary risk from food sources alone is below the Agency's level of concern for chronic risk.**

References

The following EPA memoranda have been referenced in this document.

Revised Occupational and Residential Reregistration Eligibility Document For Phorate; (August 1999); Case # 818957, PC Code 057201, DP Barcode D256244; from Jeff Dawson (OPP/HED/RRB-1) to Christine Olinger (OPP/HED/RRB-1)

Phorate: Completion of response to comments from American Cyanamid Co.; Revision of exposure estimates for surface and ground water; Updated EFED RED chapter; (August 1999); DP BARCODE: D251987; from Jim Breithaupt and David Farrar (OPP/EFED) to Ben Chambliss and Stephanie Willett (OPP/SRRD)

Phorate: Revised HED Chapter of the Reregistration Eligibility Decision Document; (February, 1999) Chemical ID No. 057201, Case 0103, DP Barcode D220565; from Christine Olinger (OPP/HED/RRB-1) to Ben Chambliss (OPP/SRRD)

Phorate. List A Reregistration Case No. 0103/Chemical ID No. 057201. HED Probabilistic (Monte Carlo) Acute Dietary Exposure and Risk Analysis (February 1999); DP Barcode No. D253139; from Christina Swartz (OPP/HED/RRB-1) to Ben Chambliss and Stephanie Willett (OPP/SRRD) and Christine Olinger (OPP/HED/RRB-1)

PHORATE: Evaluation of Revised Probabilistic Acute Dietary Risk Analyses ; (February 1999); Case #0103, PC Code 057201, Barcode D251144, MRID No.: 44695401; from Christine Olinger (OPP/HED/RRB-1) to Ben Chambliss and Stephanie Willett (OPP/SRRD)

Phorate (057201) Evaluation of Novigen Chronic and Acute Monte-Carlo Analyses ; (January 1998); DP Barcode: D241656, Rereg. Case No. 0103; from David J. Miller (OPP/HED/CEB2) to Christine Olinger (OPP/HED/RRB-1)

Quantitative Usage Analysis; (January, 1998) completed by Jihad Alsadek (EPA/OPP/BEAD)



13544

R165441

Chemical Name: Phorate

PC Code: 057201

HED File Code: 61700 SRRD REDs

Memo Date: 8/31/1999

File ID: DPD259262

Accession #: 000-00-8015

HED Records Reference Center
3/18/2009