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April 16, 1996

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MEMORANDUM

SUBJECT: **PHORATE:** The HED Chapter of the Reregistration Eligibility Decision Document (RED), Case #0103, PC Code 057201

From: Jane Smith, Chemist *Jane Smith*
Risk Characterization and Analysis Branch
Health Effects Division 7509C

Thru: Michael Metzger, Acting Branch Chief *Michael Metzger*
Risk Characterization and Analysis Branch
Health Effect Division 7509C

and
Stephanie Irene, Ph.D., Acting Director *Stephanie Irene*
Health Effects Division 7509C

To: Jill Bloom
Special Review Branch
Special Review and Reregistration Branch 7508

The Human Health Assessment for the Reregistration Eligibility Document for phorate is attached. This chapter includes the Hazard Assessment from Yung Yang in Toxicology Branch II, the Occupational/Residential Exposure Assessment from Olga Odiott in OREB, the Dietary Exposure Assessment, Product Chemistry and Tolerance Reassessment from David Miller in Chemistry Branch II, and the Dietary Risk Assessment from Brian Steinwand in DRES.

The label recommendations and labeling rationales concerning the Worker Protection Standard for Sections IV and V of the RED will be addressed later when we are certain they are necessary.

Summary of Confirmatory Data Requirements / Label Changes / Significant Items

- 1) A combined reproductive-developmental neurotoxicity study is required.
- 2) Oral acute and subchronic studies in rats and a six month study in dogs, rabbits, or monkeys to determine ocular effects are required.
- 3) A neurotoxicity screening battery (acute and subchronic) is required. It should be noted this subchronic neurotoxicity study can be conducted in a combined reproductive-developmental neurotoxicity study of this chemical
- 4) Label amendments are required. The restriction against the feeding of sugar beet tops or silage to dairy cattle is considered impractical 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



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MEMORANDUM

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TOXIC SUBSTANCES

SUBJECT: Phorate - Toxicology Chapter of the RED

TO: Paula A. Deschamp / Jane S. Smith
RCAB
Health Effect Division (7509C)

FROM: Yung G. Yang, Ph.D. *Yung G. Yang 3/5/96*
Toxicology Branch II, Section II
Health Effect Division (7509C)

THRU: K. Clark Swentzel *K. Clark Swentzel 3/5/96*
Section Head, Section II
Toxicology Branch II, HED (7509C)
and
Stephanie R. Irene, Ph.D. *Stephanie R. Irene 3/5/96*
Acting Branch Chief
Toxicology Branch II, HED (7509C)

DP Barcode: D220566
Case: 818957
Submission: S496230
Chemical: Phorate
Caswell No.: 660
PC No.: 057201
Registrant: American Cyanamid Co.

ACTION REQUEST: Prepare TOX Chapter for phorate RED.

RESPONSE: Based on the currently available toxicology data on phorate, a toxicology chapter on this chemical for the RED has been prepared and is attached.

The toxicology data base is not complete, there are data gaps which include (1) a combined reproductive-developmental neurotoxicity study in rats (Guidelines 83-4 & 82-5), (2) an acute neurotoxicity (Guideline 81-8), and (3) ocular toxicity studies. These studies are required as confirmatory data.



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TOXICOLOGY CHAPTER - PHORATE

The toxicology profile for phorate is summarized in Table 1. The toxicology data base is not complete, there are data gaps which include (1) a combined reproductive-developmental neurotoxicity study in rats (Guidelines 83-4 & 82-5), (2) an acute neurotoxicity (Guideline 81-8), and (3) ocular toxicity studies. These studies are required as confirmatory data.

Table 1. Toxicology Profile for Phorate				
Guideline	Study Type	MRID#	Required	Satisfied
81-1	Acute oral - rats	00126343	Yes	Yes
81-2	Acute dermal - rats	00126343	Yes	Yes
81-3	Acute inhalation- rats	00126343	Yes	Yes
81-4	Primary eye irritation	NA*	Yes	Waived
81-5	Primary dermal irritation	NA*	Yes	Waived
81-6	Dermal sensitization	NA*	Yes	Waived
82-1	Subchronic feeding	00092873**	Yes	Waived
82-2	Subchronic dermal	NA*	Yes	Waived
83-5	Chronic toxicity/ carcinogenicity- rats	00125233	Yes	Yes
83-1(b)	Chronic toxicity- dogs	40174527	Yes	Yes
83-2(a)	Carcinogenicity- mice	00124845	Yes	Yes
83-3(a)	Developmental toxicity- rats	00122775	Yes	Yes
83-3(b)	Developmental toxicity- rabbits	40174528	Yes	Yes
83-4	2-generation reproduction- rats	00092853***	Yes	No
84-2(a)	Gene mutation	00124901 00151633	Yes	Yes
84-2(b)	Chromosomal aberration	00124901 00155597	Yes	Yes
84-4	Other genotoxic effects	00124901	Yes	Yes
85-1	Metabolism	40291601 41803803	Yes	Yes
81-8 82-5	Neurotoxicity	NA	Yes	No
	Ocular toxicity	NA	Yes	No

* The requirements were waived due to high toxicity of the chemical.

** The study was classified as supplementary; however, it is not required to repeat the study because chronic toxicity data are available.

*** The 3-generation reproduction study in mice was down-graded from core-minimum to unacceptable by the HED RfD Peer Review Committee (December 30, 1993).

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 data base are adequate for acute toxicity of phorate. Table 2 summarizes acute toxicity values and categories for phorate.

Table 2. Acute Toxicity Values for Phorate*		
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	N/A
Dermal Irritation	Waived	N/A
Dermal Sensitization	Waived	N/A

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

Technical phorate is highly toxic on an acute oral, dermal, or 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 81-1).

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 81-2). In addition, a dermal LD₅₀ of 415.6 mg/kg in guinea pigs with typical cholinergic signs noted at higher doses were also reported (Shaffer, 1960; Baron, 1968; MRID# 00139479).

The acute inhalation LC₅₀s for rats were 0.06 and 0.011 mg/L³ 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 81-3).

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, ChE, inhibition) was satisfactorily identified, also sufficient data from chronic toxicity studies in rodents and non-rodents were available, additional data from subchronic toxicity studies are not required.

In a 90-day feeding study in rats (Tusing, 1956; MRID# 0092873), phorate were administered in the diet at dosage levels of 0.22, 0.66, 2.0, 6.0, 12.0, and 18.0 ppm (equivalent to 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 NOEL was 0.66 ppm (0.033 mg/kg/day) and the LOEL was 2 ppm (0.1 mg/kg/day) based on cholinesterase inhibition. The study was classified as supplementary because the study was flawed in that histopathology was performed on 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 0.01, 0.05, 0.25, 1.25, and 2.5 mg/kg/day, 6 days/week for 13-15 weeks. Each group had 3 dogs (2 males and 1 female) with the exception of the 2.5 mg/kg group, which had 2 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 NOEL was 0.01 mg/kg/day and the LOEL was 0.05 mg/kg/day based on the reduction of plasma ChE activity. This study was classified as supplementary because only three dogs (2 males and 1 female) per group were used instead of 4 dogs of each sex per group.

No data are available from 21-day or 90-day dermal toxicity studies with phorate. These study requirements were waived since the highly toxic nature of phorate prohibits the administration of dosages that could induce adverse effects other than inhibition of cholinesterase activity (US EPA, 1988).

C. Chronic Toxicity and Carcinogenicity

a. Combined chronic toxicity and carcinogenicity studies in rats

In a combined two-year chronic toxicity/carcinogenicity study in rats, phorate was fed to rats (50/sex/group) at dosage levels of 0,

1, 3, or 6 ppm (equivalent to 0, 0.05, 0.15, or 0.3 mg/kg/day, respectively) for 24 months. A NOEL for plasma ChE inhibition in males was not established since the LOEL was 0.05 mg/kg/day (LDT). The NOEL for plasma ChE inhibition in females was 0.05 mg/kg/day while the LOEL was 0.15 mg/kg/day. The NOEL for RBC ChE inhibition was 0.3 mg/kg/day (HDT) in males and 0.15 mg/kg/day in females while the LOEL for females was 0.3 mg/kg/day. The NOEL for brain ChE inhibition was 0.15 mg/kg/day in males and 0.05 mg/kg/day in females while the LOELs 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 83-5, 83-1a, and 83-2a).

b. Chronic toxicity study in dogs (1-year)

Groups of beagle dogs (6/sex/group) were fed phorate via capsules at doses of 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 NOEL was 0.05 mg/kg/day and the LOEL was 0.25 mg/kg/day based on body tremors in males and females and inhibited body weight gains in males. The NOEL for plasma ChE inhibition was 0.01 mg/kg/day while the LOEL was 0.05 mg/kg/day for both sexes. The NOEL for RBC or brain ChE inhibition was 0.05 mg/kg/day while the LOEL was 0.25 mg/kg/day for both sexes (Shellenberger and Tegeris, 1987; MRID# 40174527; satisfies Guideline 83-1b).

c. Carcinogenicity study in mice

Groups of CD-1 mice (50/sex/group) received phorate at a dietary concentration of 1, 3, or 6 ppm (equivalent to 0.15, 0.45, or 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 NOEL was 0.45 mg/kg/day and the LOEL 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 83-2(b)).

D. Reproduction and Developmental Toxicity Studies

a. 2-Generation reproduction Study (Rats)

No acceptable data are available to support the requirement for reproductive toxicity in rodents (Guideline 83-4). There was a 3-generation reproductive study in mice (MRID# 00092853) submitted to the Agency. In this study, technical phorate was administered in the diet to mice at dietary levels of 0.6, 1.5, and 3.0 ppm (equivalent to 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 generation 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 F_{1b} at the highest dose level. The NOEL was estimated to be 1.5 ppm (0.23 mg/kg/day) and the LOEL 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). There was only limited evidence, based on available data, to suggest that this chemical was associated with significant reproductive and developmental toxicity. However, since phorate is a potent cholinesterase inhibitor, the RfD committee recommended that a combined reproductive-developmental neuro-toxicity study should be required to support the re-registration of this chemical.

b. Developmental toxicity study in rats

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 0.125, 0.25, or 0.5 mg/kg/day. No developmental effects were observed in this study at any dosage. The NOEL for both maternal toxicity and developmental toxicity was 0.25 mg/kg/day. The LOEL 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 resulting from the anticholinesterase activity of phorate and not a true developmental effect (Beliles, 1979; MRID# 00122775; satisfies Guideline 83-3a).

c. Developmental toxicity study in rabbits

Groups of pregnant rabbits (20/group) were administered 0.15, 0.5, 0.9, and 1.2 mg/kg/day of phorate by gavage on days 6-18 of gestation. The maternal NOEL was 0.15 mg/kg/day and the maternal LOEL was 0.5 mg/kg/day based on body weight loss and increased mortality. The developmental NOEL was 1.2 mg/kg/day (the highest dose tested). No developmental effects were observed (Schroeder, 1987; MRID# 40174528; satisfies Guideline 83-3b).

E. Mutagenicity Studies

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.

a. Gene mutation

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).

b. Chromosomal aberration assay

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 dosages up to 2.5 and 1.5 mg/kg in males and females, respectively (Ivett, 1986; MRID# 00155597).

c. Other genotoxic effects

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 did not show mutagenic response (Simmon et al., 1977; MRID# 00124901).

F. 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 sulfonyl) methyl-sulfine 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).

G. Neurotoxicity Studies

a. Acute delayed neurotoxicity

In an acute 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).

b. Acute and subchronic neurotoxicity studies

No data are available on the acute and subchronic neurotoxicity of phorate. Since phorate is an organophosphate, **a neurotoxicity screening battery (acute and subchronic) is required to support the re-registration of this chemical.** Note: subchronic neurotoxicity study can be conducted in a combined reproductive-developmental neurotoxicity study of this chemical.

H. Special Studies

a. Eye Effects

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) indicates 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 requirement for ocular testing is based on the significance of the potential toxic effect, the report from Japan concerning the effects of OPs on humans and animals, a report to the Agency on ocular effects from chronic studies of methyl parathion, ethyl parathion and tribufos (DEF), and our general lack of routine and sensitive testing for ocular effects. Thus, **acute and subchronic studies in rats and a six month study in dogs, rabbits, or monkeys for phorate are required to support the re-registration of this chemical.**

b. Phorate Metabolite

Phorate sulfoxide (a phorate metabolite) was administered to rats (35/sex) at dietary levels of 0.32, 0.8, and 2.0 ppm (equivalent to

0.016, 0.04, and 0.10 mg/kg, respectively) for 90 days. 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 NOEL was 0.32 ppm (0.016 mg/kg) and the LOEL was 0.8 ppm (0.04 mg/kg) based on inhibition of plasma and RBC ChE activities (Hutchison et al., 1968; MRID# 00092912).

Methane (ethylsulfonyl) (methylsulfonyl), a phorate metabolite, 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. However, findings of the rat metabolism study showed that the oxidative, phosphorylated products represented minor proportions of the phorate metabolites measured in tissues, feces, and urine. Additional toxicity studies with the oxidative metabolites may be required, if significant residue levels are detected in the required residue studies.

I. Toxicity Endpoint Selection for Risk Assessment

Cholinesterase inhibition in RBCs and brain from a one-year feeding study in dogs was selected as an endpoint for acute dietary risk assessment and for both short and long term occupational and residential exposure risk assessment. A NOEL dose of 0.05 mg/kg/day is used for the risk assessment. The LOEL was 0.25 mg/kg/day based on inhibition of RBC and brain ChE.

J. Reference Dose (RfD)

The RfD for phorate was established as 0.0005 mg/kg/day based on a NOEL of 0.05 mg/kg/day in a one-year feeding study in dogs. The LOEL was 0.25 mg/kg/day based on depression of RBC and brain ChE activity and observation of body tremors in both sexes. An uncertainty factor of 100 was used to account for differences between species and variability between humans. It should be noted that a regulatory value (ADI) of 0.0002 mg/kg/day was established for phorate by the World Health Organization (WHO) in 1985.

REFERENCES

MRID No.

- 00092853 Morici, I.J.; Shaffer, C.B.; Ribelin, W.E.; et al. (1956) Thi-met[^](R) Systemic Insecticide: Successive Generation Studies with Mice: Report No. 65-136. (Unpublished study received on unknown date under PP0378; submitted by American Cyanamid Co. Princeton, NJ; CDL:092662-A).
- 00092873 Tusing, T.W. (1956) Progress Report: Repeated Oral Administration--Dogs. (Unpublished study, including letter dated Jan 25, 1956 from T.W. Tusing to D.O. Hamblin, Received Feb 20, 1956 under 241-36; prepared by Hazelton Laboratories, submitted by American Cyanamid Co., Princeton, NJ; CDL:092661-M).
- 00092912 Hutchison, E.B.; Fegley, H. C.; McNerney, J.M. et al. (1968) Sulfoxide of Thimet Systemic Insecticide: Ninety-day Repeated Feeding to Albino Rats: CL 18,177: Report No. 68-65. (Unpublished study received Jul 25, 1968 under 8F0673; submitted by American Cyanamid Co., Princeton, NJ; CDL:092974-E)
- 00122775 Beliles, R. (1979) Teratology Study in Rats: Thimet Phorate: LBI Project No. 20819. Final report. (Unpublished study received Dec 30, 1982 under OE2391; prepared by Litton Bionetics, submitted by American Cyanamid Co., Princeton, NJ; CDL:071330-A; 071331)
- 00124845 Manus, A.; Goldsmith, L. Sekerke, H.; et al. (1981) 18-month Chronic Toxicity and Potential Carcinogenicity Study in Mice: Phorate: LBI Project No. 20820. Final report. (Unpublished study received Oct 13, 1982 under 241-53; prepared by Litton Bionetics, Inc., submitted by American Cyanamid Co., Princeton, NJ; CDL:248780-A).
- 00124901 Simmon, V.; Mitchell, A.; Jorgenson, T. (1977) Evaluation of Selected Pesticides as Chemical Mutagen: In vitro and in vivo studies: EPA-600/1-77028: Pre RPAR Review Submission #3 (Unpublished study received Sep 14, 1977 under 1471-35; Prepared by Stanford Research Institute, Environmental Toxicology Div., Health Effects Research Laboratory, and U.S. Environmental Protection Agency, Office of Research and Development, submitted by Elanco Products Co., Div. of Eli Lilly and Co., Indianapolis, IN; CDL:233222-L.
- 00125233 Manus, A.; Goldsmith, L.; Maloney, D.; et al. (1981) 24-month Chronic Toxicity and Potential Carcinogenicity Study in Rats: Phorate: LBI Project No. 20821. Final report. (Unpublished study received Oct 13, 1982 under 241-53; prepared by Litton Binetics, Inc., submitted by American Cyanamid Co., princeton, NJ; CDL:248778-A; 238779).
- 00126343 Newell, G.; Dilley, J. (1978) Teratology and Acute Toxicology of Selected Chemical Pesticides Administered by Inhalation. By Stanford Research Institute. Research Triangle Park, NC; U.S. Environmental Protection Agency, Office of Research and Development, Health Effects Research Laboratory. (EPA-600/1-78-

(11)

003; contract no. 68-02-1751; available from: NTIS: PB277077; also in unpublished submission received Mar 10, 1983 under 352-325; submitted by E.I. du Pont de Nemours & Co., Inc., Wilmington, DE; CDL:249679-I)

- 00139479 Shaffer, C.B. (1960) Thimet and Formulations: Toxicity by Skin Absorption: Report No. 58-11. (Unpublished study received on unknown date under admin. no.; submitted by American Cyanamid Co. Princeton, NJ.; CDL:103661-F.
- 00151633 Thilagar, A. (1985) Test for Chemical Induction of Gene Mutation at the HGPRT Locus in Cultured Chinese Hamster Ovary (CHO) Cells with and without Metabolic Activation: AC 35,024: Sitek's Study No. 0007-2500. Unpublished. American Cyanamid Co. Study No. 980-85-133 prepared by Sitek Research Laboratories. 53p.
- 00152640 Fletcher, D. (1984) 42-day Neurotoxicity Study with Phorate in Mature White Leghorn Chickens:BLAL No. 83 DN103. Unpublished study prepared by Bio-Life Associates, Ltd. 51p.
- 00155597 Ivett, J. (1986) Chromosomal Aberrations in vivo in Mammalian Bone Marrow Cells on AC35,024: Second Amended Final report: LBI Project No. 22202. Unpublished study prepared by Litton Bionetics. 50p.
- 40174526 Lowe, C.; Fischer, J. (1987) Acute Oral Toxicity of AC 180,296-- A metabolite of AC35,024 in Male and Female Rats: Report No. A87-11. Unpublished study prepared by American Cyanamid Co., 5p.
- 40174527 Shellenberger, T.; Tegeris, A. (1987) One-year Oral Toxicity Study in Purebred Beagle Dogs with AC35024: Laboratory Project Id: 85015. Unpublished study prepared by Tegeris Laboratories, Inc. 881p.
- 40174528 Schroeder, R. (1987) A Teratology Study with Phorate in Rabbits: Project No. 86-3039. Unpublished study prepared by Bio/Dynamics, Inc. 359p.
- 40291601 Hussain, M. (1987) Timet Insecticide, Phorate (CL 35, 024): Disposition and Metabolic Fate of Carbon-14 Labeled CL35, 024 in the Rat: General Metabolism-- Rat: Project No. 0109; Report No. PD-M Volume 24-23. Unpublished study prepared by American Cyanamid Co. 135p.
- 41803803 Miller, P.; Wu, D. (1991) Phorate (CL 35,024) (Phorate/20G): Adsorption, Distribution, Elimination, and Metabolic Fate of Carbon-14 CL 35,024 in the Female Rat: Lab Project No. 27-59:RPT0043. Unpublished study prepared by American Cyanamid Company 127p.

U.S. Environmental Protection Agency (December, 1988);
Registration Standard for the Registration of Pesticide Products
Containing Phorate as the active Ingredient. OMB Control No.
2070-0057.