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ORGANISATION POUR L'ALIMENTATION ET L'AGRICULTURE

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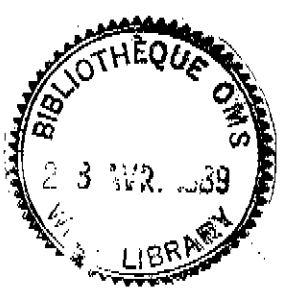
DATA SHEET ON PESTICIDES

No. 75

PHORATE



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CLASSIFICATION:

Primary use: Insecticide

Secondary use: Acaricide, nematocide

Chemical group: Organophosphorus compound

Date issued: July 1988

1.0 GENERAL INFORMATION

1.1 COMMON NAME: phorate (E-ISO, F-ISO, BSI ANSI, ESA), timet (U.S.S.R.)

1.1.1 Identity:

IUPAC: O,O-diethyl S-ethylthiomethyl phosphorodithioate

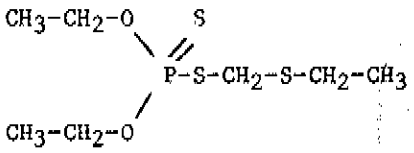
CAS: O,O-diethyl S-[(ethylthio)methyl] phosphorodithioate

CAS Reg. No.: 298-02-2

Molecular formula: $C_7H_{17}O_2PS_3$

Relative molecular mass: 260.4

Structural formula:



1.1.2 Synonyms: AC 3911, Agrimet^R, CL 35024, EI 3911, ENT 24 042, foraat, Geomet^R, Granutox^R, L 11/6, phorat, Rampart^R, Thimenox^R, Thimet^R, timet, Vergfru Foratox^R.

1.2 SYNOPSIS: Phorate is a broad spectrum, non-biocumulative organophosphorus insecticide and acaricide, an indirect inhibitor of cholinesterase with good contact, stomach and fumigant action against target organisms. It is extremely toxic to mammals and other non-target organisms. It is a plant systemic with no residual action. Granular formulations are most commonly used. The sulphone metabolite may persist in soil, and relatively long pre-harvest intervals are recommended.

1.3 SELECTED PROPERTIES

1.3.1 Physical characteristics: Phorate is a clear, pale yellow mobile liquid. It has a boiling point of 118-120 °C (107 Pa), and a freezing point of -42.9 °C; a density (d^{25}) of 1.167. The technical material is over 90% pure.

1.3.2 Solubility: Water, 50 mg/L at 25 °C; miscible with carbon tetrachloride, dioxane, vegetable oils, xylene, alcohols, ethers and esters.

1.3.3 Stability: Phorate is stable for at least two years at room temperature in media between pH 5 and 7. In very acidic (pH <2) or very alkaline (pH >9) media, hydrolysis occurs at rates dependent upon pH and temperature.

1.3.4 Vapour pressure: 85 mPa (25 °C)

1.4 AGRICULTURE, HORTICULTURE AND FORESTRY

1.4.1 Common formulations: Emulsifiable concentrates of various concentrations including 960 g tech./L and 250 g a.i./L are still available, however, granular formulations containing 50, 100, 150, 200 g a.i./kg are almost universally used.

1.4.2 Susceptible pests: Mites, aphids, greenbugs, thrips, leafhoppers, sorghum shootfly, leafminers, corn rootworms, psyllids, cutworms, Hessian fly, foliar nematodes, wireworms, flea beetles, whiteflies, pine tip moth, and others.

1.4.3 Use pattern: Phorate may be used in foliar or soil treatments on alfalfa, barley, beans, brassicas, coffee, corn, cotton, grapes, hops, lettuce, oats, peanuts, potatoes, rice, sorghum, soybeans, sugar cane, sugar beets, tomatoes, watermelon, wheat and on ornamentals and pine nursery stock.

Soil applications may be applied as a band treatment on each side of the seed row or incorporated into the soil as a side dress, irrigation should follow as soon as possible. Care should be taken to avoid contact with seed in the furrow. In foliar treatments apply under dry conditions into plant crowns as insects appear.

1.4.4 Unintended effects: Phorate is toxic to many seeds and to many non-target organisms, including bees and fish. Contamination of standing water and waterways must be avoided. Good agricultural practices and the use of granular formulations diminish these adverse effects.

1.5 PUBLIC HEALTH USE: No recommended use.

1.6 HOUSEHOLD USE: No recommended use.

2.0 TOXICOLOGY AND RISKS

2.1 TOXICOLOGY - MAMMALS

2.1.1 Absorption route: Phorate may be absorbed from the gastrointestinal tract, through the intact skin and by inhalation of spray mists or fine dust.

2.1.2 **Mode of action:** Several metabolites of phorate inhibit the activity of both acetylcholinesterase and pseudocholinesterase.

2.1.3 **Metabolism and excretion products:** Phorate is metabolized in animals to yield phorate sulphoxide and phorate sulphone and the oxygentated analogues (phoratoxon, phoratoxone sulphoxide and phoratoxone sulphone) which are excreted as diethyl phosphoric acid, O-O-diethyl phosphorothioic and O-O-diethylphosphorodithioic acid.

Oral administration of a single dose of 2 mg/kg of labelled phorate to rats resulted in 35% of material being excreted in urine and 3.5% in the faeces, within six days.

Six daily doses of 1 mg/kg/day of phorate to rats resulted in 12% and 6% being excreted in the urine and faeces respectively within seven days. At necropsy brain, liver and kidney tissue contained unidentified and largely unextractable residues.

2.1.4 **Toxicity, single dose** (technical material)

Oral LD_{50}:

Rat (M)	2.3-3.2 mg/kg b.w.
Rat (F)	1.1-1.6 mg/kg b.w.
Mouse (M,F)	3.5-6.5 mg/kg b.w.

Dermal LD_{50}:

Rat (M)	5.7-9.3 mg/kg b.w.
Rat (F)	2.5-3.9 mg/kg b.w.
Rabbit	5.2 mg/kg b.w.

Inhalation LC_{50}:

Rat (M)	60 mg/m^3 (1 hour)
Rat (F)	11 mg/m^3 (1 hour)

I.V. LD_{50}:

Rat (M)	2.2 mg/kg b.w.
Rat (F)	1.2 mg/kg b.w.

I.P. LD_{50}:

Rat	1.98 mg/kg b.w.
Mouse	3.0 mg/kg b.w.

2.1.5 **Toxicity, repeated doses**

Oral: Mongrel dogs given 0.05 mg/kg/day for 15 weeks had significantly depressed plasma and erythrocyte cholinesterase activity. At 2.5 mg/kg two dogs died following a single dose.

2.1.6 Dietary studies

Short term: The plasma, erythrocyte and brain cholinesterase activity of rats fed on a diet containing phorate at levels greater than 0.66 ppm was depressed. In rats fed on a diet containing up to 6 ppm of phorate no effect on growth, food consumption, or histopathology was noticed.

Long term: In a two year rat dietary study at dose levels of 1, 3 or 6 ppm, growth was depressed at the highest dose level, among females only, and only 36% of animals in this group survived terminally. Erythrocyte cholinesterase activity was not affected at any dose level whereas plasma cholinesterase activity was depressed at 6 ppm in males and at 3 and 6 ppm in females.

In an 18 month study in mice fed on a diet containing phorate 1, 3 or 6 ppm, growth was retarded in females at 6 ppm. However, in all dose groups food aversion was observed for both sexes. There were no observed compound related adverse effects other than clinical signs of cholinesterase inhibition.

2.1.7 Supplementary studies of toxicity

Carcinogenicity: Results of rat and mouse chronic toxicity studies have not demonstrated any carcinogenic potential for phorate.

Mutagenicity: Phorate was not mutagenic in a dominant lethal test in mice and in several microbial systems including Salmonella typhimurium (reverse mutation), Saccharomyces cerevisiae (mitotic recombination) and in several Ames tests with E. coli and B. subtilis.

Teratogenicity: In a rat study phorate was not observed to be teratogenic at oral doses up to 0.25 mg/kg/day. At 0.5 mg/kg/day (high dose level), an increased incidence of hypertrophy of the heart was observed. In another rat study, exposure to phorate by inhalation at the dose of 1.94 mg/m^3/day, during the seventh through fourteenth day of gestation, caused increased foetal mortality and decreased foetal weight gain but teratogenic effects were not observed.

Reproduction: In a three generation study in mice, with phorate levels in diet up to 3 ppm, no compound related effects on the fertility, gestation, viability or lactation indices were observed.

Neurotoxicity: Phorate produced no adverse effects on nerve fibres or the myelin sheath in hens fed dietary levels of 40 ppm for four weeks. In a separate study no delayed neurotoxicity was noted in hens given phorate as a single dose of 14.2 mg/kg.

2.1.8 Modification of toxicity: No potentiation of toxicity was observed in male rats treated with equitoxic portions of phorate and each of 10 other pesticides.

2.2 TOXICOLOGY - MAN

2.2.1 Absorption route: Phorate may be absorbed from the gastrointestinal tract, through the intact skin, or by inhalation of dust.

2.2.2 Dangerous doses

Single: 5 mg/kg b.w.

Repeated: Not known

2.2.3 Observations in occupationally exposed workers: There have been no reports of fatalities associated with the use of phorate. A 16 year old youth became ill after working with phorate treated cotton seed. Symptoms included coma, undetectable blood pressure, pinpoint pupils, blood tinged frothy sputum and occasional convulsions. One day after onset, erythrocyte and plasma cholinesterase activities were 21% and 49% of normal respectively. Two illnesses occurred in the same formulating plant where phorate concentrations in the air were measured at 0.07-14.60 mg/m^3. In another incident, a formulator experienced neurological symptoms following exposure to phorate while cleaning a mixing tank. This was accompanied by a 50% reduction in plasma and erythrocyte cholinesterase and increased urinary levels of diethyl phosphate, a metabolite of phorate.

2.2.4 Observations on exposures of the general population: No published information available. However, when recommended agricultural practices are followed no adverse effects are expected.

2.2.5 Observations on volunteers: No published information available.

2.2.6 Reported mishaps: No published information available.

2.3 TOXICOLOGY TO NON MAMMALIAN SPECIES

2.3.1 Birds

Oral LD_{50} (technical material):

Mallard (F)	0.62-2.55 mg/kg b.w.
Pheasant (F)	7.12 mg/kg b.w.
Chukar (F)	12.8 mg/kg b.w.
Red-winged blackbird	1.00 mg/kg b.w.
Starlings	7.5 mg/kg b.w.
Grackles	1.30 mg/kg b.w.

Dermal LD_{50} (technical material):

Mallard (F)	203 mg/kg b.w.

Dietary LD_{50} (5 day):

Bobwhile quail	373 ppm
Japanese quail	200 ppm
Ring-necked pheasant	441 ppm
Mallard	248 ppm

2.3.2 Fish: Highly toxic to fish

Bluegill TLM	5.5 µg/L (48 hour)	technical material
Rainbow trout LC_{50}	13.0 µg/L (96 hour)	technical material
Channel catfish LC_{50}	280.0 µg/L (96 hour)	technical material

2.3.3 Other species: Highly toxic to bees

Oral LD_{50}:

Bullfrog (F)	85.2 mg/kg b.w. (technical material)

3.0 FOR REGULATORY AUTHORITIES - RECOMMENDATIONS ON REGULATION OF COMPOUND

3.1 RECOMMENDED RESTRICTIONS ON AVAILABILITY

(For definition of categories see the Introduction to Data Sheets.)

Liquid formulation of 10% and over, Category 1.

Other liquid formulations, Category 2.

Solid formulations of 40% and over, Category 1.

Other solid formulations, 4-40%, Category 2, less than 4%, Category 3.

3.2 TRANSPORTATION AND STORAGE

All formulations: Phorate should be transported and stored in clearly labelled impermeable containers under lock and key, secure from access by children and other unauthorized persons. No food or drink should be stored in the same compartment.

3.3 HANDLING

All formulations: Full protective clothing (see 4.3) should be used by those handling the compound. Adequate washing facilities should be available at all times during the handling and should be close to the site of handling. Eating, drinking and smoking should be prohibited during handling and prior to washing after handling.

3.4 DISPOSAL AND/OR DECONTAMINATION OF CONTAINERS

All formulations: Container must first be decontaminated and then crushed and buried below topsoil. Care must be taken to avoid subsequent contamination of water sources. Decontamination of containers in order to use them for other purposes should not be permitted.

3.5 SELECTION, TRAINING AND MEDICAL SUPERVISION OF WORKERS

All formulations: Pre-employment medical examination of workers is necessary. Workers suffering from active hepatic or renal disease should be excluded from contact. Pre-employment and periodic blood cholinesterase tests for workers is desirable. Special account should be taken of the worker's mental ability to comprehend and follow instructions. Training of workers in techniques to avoid contact is essential.

3.6 ADDITIONAL REGULATIONS RECOMMENDED IF DISTRIBUTED BY AIRCRAFT

All formulations: Not recommended for aerial application.

3.7 LABELLING

All formulations

"DANGER - POISON"
(skull and cross-bones insignia)

Phorate is an organophosphorus compound which inhibits cholinesterase. It is extremely toxic. Contact with the skin, inhalation of dust or spray, or swallowing may be fatal. Wear protective gloves, clean protective clothing, and a respirator of the organic-vapour type when handling this material. Wash immediately after work. Ensure that containers are stored under lock and key. Empty containers must be disposed of in such a way as to prevent all possibility of accidental contact with them. Keep the material out of reach of children and well away from foodstuffs, animal feed and their containers.

In case of contact, immediately remove contaminated clothing and wash the skin thoroughly with soap and water; for eyes, flush with water for 15 minutes.

If poisoning occurs, call a physician. Atropine sulfate is the principal antidote, repeated doses may be necessary. Pralidoxime chloride (2-PAM or protopam chloride) may be effective as an adjunct to atropine treatment. Artificial respiration also may be needed.

3.8 RESIDUES IN FOOD

Maximum residue levels: Maximum residue levels were estimated by the Joint FAO/WHO Meeting on Pesticide Residues in 1984 for several commodities as temporary.

4.0 PREVENTION OF POISONING IN MAN AND EMERGENCY AID

4.1 PRECAUTIONS IN USE

4.1.1 General: Phorate is an extremely toxic organophosphorus pesticide. It penetrates the intact skin and is also absorbed by inhalation and from the gastrointestinal tract. Repeated exposure may have a cumulative effect on the cholinesterase activity. Most formulations should be handled by trained personnel wearing protective clothing.

4.1.2 Manufacture and formulation - T.L.V.: 0.05 mg/m^3 (TWA); 0.2 mg/m^3 (STEL) for skin absorption. Closed systems and forced ventilation may be required to reduce, as much as possible, the exposure of workers to the chemical.

4.1.3 Mixers and applicators: When opening the container and when mixing, protective impermeable boots, clean overalls, gloves and respirator should be worn. Mixing, if not mechanical, should always be carried out with a paddle of appropriate length. When spraying all crops a face mask should be worn, as well as an impermeable hat, clothing, boots and gloves. The applicator should avoid working in spray mist and avoid contact with the mouth. Particular care is needed when equipment is being washed after use. All protective clothing should be washed immediately after use, including the insides of gloves. Splashes must be washed immediately from the skin, or eyes, with large quantities of water. Before eating, drinking, smoking, hands and other exposed skin should be washed.

4.1.4 Other associated workers: Persons exposed to the compound and associated with its application should wear protective clothing and observe the precautions described above in 4.1.3 under "mixers and applicators".

4.1.5 Other populations likely to be affected: Respecting good agricultural practice, subject to 4.2 below, other persons should not be exposed to hazardous amounts of the compound.

4.2 ENTRY OF PERSONS INTO TREATED AREA

Unprotected persons should be kept out of tall crops for four days and out of other crops for 24 hours.

4.3 DECONTAMINATION OF SPILLAGE AND CONTAINERS

Residues in containers should be emptied in a diluted form into a shallow pit, taking care to avoid contamination of ground waters. The empty container may be decontaminated prior to disposal by rinsing two or three times with water and scrubbing the sides. Impermeable gauntlets should be worn during this work, and a soakage pit should be provided for the rinsings. Decontamination of containers in order to use them for other purposes including storage of food and drink should not be permitted. Spillage of the compound and its formulations should be removed by washing with 5% sodium hydroxide solution and then rinsing with large quantities of water.

4.4 EMERGENCY AID

4.4.1 Early symptoms of poisoning: Early symptoms of poisoning may include tightness of chest, non-reactive pinpoint pupils, excessive sweating, headache, weakness, giddiness, nausea, vomiting, hypersalivation, diarrhoea, abdominal pains, blurred vision, slurred speech and muscle twitching. Advanced symptoms are: convulsions, coma, loss of reflexes and loss of sphincter control.

4.4.2 Treatment before person is seen by a physician, if these symptoms appear following exposure: The person should stop work immediately, remove contaminated clothing and wash the affected skin with soap and water and flush the area with large quantities of water. If swallowed and if the person is conscious, vomiting should be induced. In the event of collapse, artificial respiration should be given, bearing in mind that if mouth-to-mouth respiration is used, vomit may contain hazardous amounts of the pesticide. Call a physician immediately and transport the patient to the nearest medical facility if necessary.

5.0 FOR MEDICAL AND LABORATORY PERSONNEL

5.1 MEDICAL DIAGNOSIS AND TREATMENT IN CASES OF POISONING

5.1.1 General information: Phorate, an organophosphorus pesticide, is extremely toxic to mammals. It is readily absorbed from the gastrointestinal tract, through the intact skin and by inhalation. It is converted *in vivo* to the oxygen analogue which inhibits cholinesterase. It does not accumulate in body tissues.

5.1.2 Symptoms and signs: Initial symptoms of poisoning may include tightness of chest, non-reactive pinpoint pupils, excessive sweating, headache, weakness, giddiness, nausea, hypersalivation, vomiting, diarrhoea, abdominal pains, blurred vision, slurred speech and muscle twitching. More advanced symptoms of poisoning may be convulsions, coma, loss of reflexes and loss of sphincter control.

5.1.3 Laboratory: The most important finding is reduction of activity of blood cholinesterases. Urinary levels of organic phosphorus containing metabolites may also be used as a measure of exposure. Neither method is specific for the compound.

5.1.4 Treatment: If the pesticide has been ingested, unless the patient is vomiting, rapid gastric lavage should be performed using 5% sodium bicarbonate, if available. In case of skin contact, the skin should be washed with soap and water. If the compound has entered the eyes, they should be washed with large quantities of isotonic saline or water.

Persons without signs of respiratory impairment but with manifest peripheral symptoms should be treated with 2-4 mg of atropine sulfate by intravenous or intramuscular injection and 1 000 mg of pralidoxime chloride or 250 mg of toxogonin (adult dose) by slow intravenous infusion. More atropine may be given as needed. Persons with severe intoxication, with respiratory difficulties, convulsions and unconsciousness should immediately be given ventilatory support followed by atropine and a reactivator. In such severe cases 4-6 mg of atropine sulfate should be given initially followed by repeated doses of 2 mg at 5-10 minute intervals. Diazepam may be given to control convulsions which are unresponsive to atropine and pralidoxime. The patient's condition including respiration, blood pressure, pulse frequency, salivation and convulsions should be carefully observed as a guide to further administration of atropine. If the patient is cyanotic artificial respiration should be given at the same time as atropine sulfate. The airways should be kept free and artificial respiration should be applied if required, preferably by mechanical means. If necessary, intubation should be performed.

Contraindications are morphine, aminophylline, phenothiazines, reserpine, furosemide or ethacrynic acid.

Pralidoxime and toxogonin alone are not regarded as effective antidotes in organophosphorus poisoning, but may be effective as an adjunct to atropine.

5.1.5 **Prognosis**: If the acute poisoning episode is survived and if needed adequate artificial respiration has been given the chances of complete recovery are good. However, in very severe cases, particularly if artificial respiration has been inadequate, prolonged anoxia may give rise to permanent brain damage.

5.1.6 **References of previously reported cases**: Phorate has been implicated in a number of cases of pesticide poisoning.

Brokopp, C.D., Wyatt, J. L and Gabica, J., Dialkyl Phosphates in Urine Samples from Pesticide Formulators to Disulfoton and Phorate. (1981), Bull. Environ. Contam. Toxicol., 26, 524-529.

Hayes, W. J. (1982), "Pesticides Studied in Man" p. 360, Williams and Wilkins, Baltimmore, USA

Young, R. J., Jung, F. P. and Ayer H. E., Phorate Intoxication at an Insecticide Formulating Plant. (1979), Amer. Indust. Hyg. Assoc. 40, 1 013-1 016.

5.2 SURVEILLANCE TESTS

Test	Normal level*	Action level*	Symptomatic level*
Plasma cholinesterase	100%	50%	variable
Whole blood or erythrocyte cholinesterase	100%	70%	usually 40%

5.3 LABORATORY METHODS

5.3.1 **Detection and assay of compound**: Product analysis is by I.R. spectroscopy. Residues of phorate and its oxidation products may be determined by GLC.

Boshoff, P.R. and Pretorius, V., (1979), J. Agric. Food Chem. 27, 626-630.

Boyd, J.G. (1972), Anal. Methods Pestic. Plant Growth Regul. Food Addit., 6, 493-510.

Brokopp, C.D., Wyatt, J. L and Gabica, J., (1981), Bull. Environ. Contam. Toxicol., 26, 524-529.

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Mount, M.E. and Oehme F. W. (1981), Vet. Hum. Toxicol., 23, 34-42.

Sans, W.W. (1978), Assoc. Off. Anal. Chem., 61, 837-840.

Stan, A.J., Abraham, B., June, J., Kellert, M., Steinland, K. (1977), Fresenius Z. Anal. Chem., 287, 271-285.

* Expressed as a percentage of pre-exposure activity.