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WHO/FAO DATA SHEET ON PESTICIDES

No. 85

d-PHENOTHRIN

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CLASSIFICATION:

Primary use: Insecticide
 Secondary use:
 Chemical group: Pyrethroid

1.0 GENERAL INFORMATION

1.1 COMMON NAME: phenothrin (BSI, E-ISO); phénothrine (F-ISO).

1.1.1 Identity

d-Phenothrin is a mixture of four stereoisomers. The technical compound is a 20:80 *cis:trans* mix of both (1R) - (1S) - configurations. The (1R) - configurations have a greater insecticidal activity than the corresponding (1S) - isomers. d-Phenothrin, a preparation rich in (1R) - isomers, with a *cis:trans* ratio 20:80, has been marketed. Data pertaining to this latter product will be designated d-phenothrin in this data sheet.

IUPAC chemical name: 3-phenoxybenzyl (1RS, 3RS; 1RS, 3SR)-2, 2-dimethyl-3-(2-methylprop-1-enyl) cyclopropanecarboxylate. The alternative nomenclature of (1RS)-*cis, trans*- has also been used to designate the stereoisomers and will be used in this data sheet.

CAS chemical name: Cyclopropanecarboxylic acid, 2,2-dimethyl-3-(2-methyl-1-propenyl)-(3-phenoxyphenyl)methyl ester.

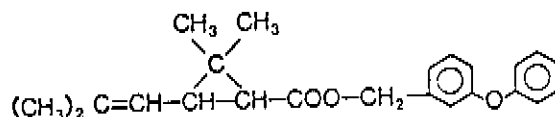
CAS registry number: 26002-80-2 (racemic).

RTECS registry number: GZ 1975000 (racemic)
 GZ 2002000 (d-phenothrin)

Molecular formula: $C_{23}H_{26}O_3$

Molecular mass: 350.5

Structural formula:



Synonyms and trade names: (1R)-phenothrin; S-2539, Multicide concentrate F-2271, Welcide^R. The (1R)-*cis, trans* (d-phenothrin); isomers (20:80) are known as Sumithrin^R; S-2539 Forte^R; Pesguard-A NS, Pesguard-A NS W, or Pesguard NS. The (R) - isomers may also be designated (+) or d-; the (S) - isomers as (-) or l-.

1.2 SYNOPSIS: d-Phenothrin is a fast acting insecticide, effective by contact and stomach action. It is rapidly metabolized and excreted by mammals and has low mammalian toxicity. Stable to storage in the dark; relatively unstable to sunlight or ultra violet irradiation, or in alkaline media.

1.3 SELECTED PROPERTIES

- 1.3.1 **Physical characteristics:** d-Phenothrin is a yellow to yellow-brown liquid, with a density of 1.061 g/cm³ (25 °C) and a refractive index of 1.5482.
- 1.3.2 **Solubility:** Soluble in water (25 °C) 2 mg/L. Soluble in organic solvents.
- 1.3.3 **Stability:** d-Phenothrin is hydrolysed by alkalis but is stable in neutral or weakly acidic media. Unstable in most solvents except methanol, ethyl cellosolve, o-cresol and dimethylsulfoxide. Unstable to ultra violet irradiation and has a short residual life on pre-harvest application. However, d-phenothrin applied to wheat after harvest showed only slight degradation after six months storage at 30 °C. When protected from light no breakdown of d-phenothrin was observed after one year at room temperature.
- 1.3.4 **Vapour pressure:** d-Phenothrin has a vapour pressure of 0.16 mPa at 20 °C.

1.4 AGRICULTURE, HORTICULTURE AND FORESTRY

- 1.4.1 **Common formulations:** Water and oil based aerosols, liquid concentrates, emulsifiable concentrates, powders and dusts. May be formulated with synergists or with other pyrethroid and non-pyrethroid insecticides.
- 1.4.2 **Pests controlled:** Controls most *Lepidoptera*, *Hemiptera* (bed bugs), *Diptera* (flies, gnats, and mosquitos), cockroaches and lice.
- 1.4.3 **Use pattern:** d-Phenothrin is a non-systemic insecticide which is effective by contact and as a stomach poison. Used for power-spray, mist, thermal fog, aerosol and ULV applications. The major use of d-phenothrin is in the control of nuisance insects and insects of importance to public health, and it is used to control human lice, in which case it is formulated as a powder, shampoo, or lotion. It is also used to protect grain.
- 1.4.4 **Unintended effects:** Toxic to fish and bees.

1.5 PUBLIC HEALTH PROGRAMMES

It is used for the impregnation of bednets and for aircraft disinsection.

- 1.5.1 **Common formulations:** As described in Section 1.4.1, but also formulated into powders, lotions and shampoos.
- 1.5.2 **Pests mainly controlled:** See section 1.4.2.
- 1.5.3 **Use pattern:** Should be used according to manufacturers' instructions on appearance of the pest.

1.6 HOUSEHOLD USE

- 1.6.1 **Common formulations:** See Sections 1.4.1 and 1.5.1 for general formulation details.
- 1.6.2 **Pests mainly controlled:** See Section 1.4.2.
- 1.6.3 **Use pattern:** See sections 1.4.3 and 1.5.3.

2.0 TOXICOLOGY AND RISKS

2.1 TOXICOLOGY - MAMMALS

- 2.1.1 **Absorption route:** Absorbed from the gastrointestinal tract and from the intact skin. The dermal absorption rate differs between the (1R)-*cis*- and the (1R)-*trans*-isomers. No data are available for the rate or extent of absorption from the lung.
- 2.1.2 **Mode of action:** d-Phenothrin is a neuropoison. The symptoms of poisoning are typical of those of pyrethroids without a cyano-substituent. The proposed mechanism of action is due to the reversible binding of d-phenothrin to the sodium channels of the neuronal membrane, in this way modifying the permeability of the membrane to ions.
- 2.1.3 **Excretion products:** No published data are available for the combined isomers of d-phenothrin. The metabolism of the individual (1R)-*cis*- and (1R)-*trans*- isomers has been investigated in the rat. For both isomers an oral dose of 10 mg/kg b.w. was metabolized by hydrolysis, oxidation and conjugation and 96% of the administered dose was recovered in the urine and faeces within six days.

Following oral administration of the (1R)-*trans*- isomer, the urine was the major excretory route. The isomer was extensively metabolized to oxidative and conjugated derivatives of the hydrolysed ester. Oxidative and conjugated derivatives of the (1R)-*cis*-isomer were also observed but hydrolysis of the ester linkage was a minor metabolic pathway. With this isomer the faeces was the major excretory route.

The metabolic profiles were similar following dermal application, although the rates of excretion for each isomer showed some differences between the two routes of administration.

2.1.4 **Toxicity, single dose:**

Oral LD₅₀

Rat	> 10,000 mg/kg b.w. (without vehicle)
Rat	> 5,000 mg/kg b.w.
Mouse	> 5,000 mg/kg b.w. (in corn oil)

Dermal LD₅₀

Rat	> 10,000 mg/kg b.w.
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Intraperitoneal LD₅₀

Rat	> 5,000 mg/kg b.w.
Mouse	> 5,000 mg/kg b.w.

Intravenous LD₅₀

Rat	452-492 mg/kg b.w.
Mouse	354-405 mg/kg b.w.

LD₅₀ (1R)-phenothrinOral

Rat > 10,000 mg/kg b.w.

Dermal

Rat > 10,000 mg/kg b.w.

Subcutaneous

Rat > 10,000 mg/kg b.w.

Inhalation LC₅₀ - 4 hour exposure (1R)-phenothrin

Rat > 3.76 g/m³

Mouse > 1.2 g m³ (1-2 µm particulates in kerosene)

No sex difference in the toxicity was reported. Following intravenous administration symptoms of poisoning included fibrillation, tremor, slow respiration, salivation, lacrimation, ataxia and paralysis. The symptoms appeared 0.5 - 1 hour after administration and diminished spontaneously.

No histopathological findings in the nervous system were observed following four hour inhalation exposure of rats to 3.76 mg/L (see Section 2.1.7).

2.1.5 Toxicity, repeated dose:

Inhalation: Sprague Dawley rats or ddY mice exposed to concentrations of less than 0.21 mg (1R)-phenothrin/L, for 4 hours/day, five days/week for four weeks, showed no adverse effect on behaviour, growth, clinical chemistry or organ histopathology.

2.1.6 Dietary studies:

Short term: A 24 week dietary administration of up to 2500 mg (1R)-phenothrin/kg diet to Sprague Dawley rats had no adverse effect on growth, haematology, biochemical or histopathological parameters. Doses more than 5000 mg/kg diet produced increased liver weights which were accompanied by histopathological changes of an unspecified nature. Rats and dogs receiving (1R)-phenothrin in the diet for six months showed no adverse effect at 1000 and 300 mg/kg diet, respectively.

Long term: A dose related increased incidence of alveolar amyloidosis was observed in Swiss mice receiving 300-3000 mg d-phenothrin/kg diet for 18 months. The increased liver weights (both sexes) and a decreased growth rate (males) were observed at 3000 mg/kg diet.

No compound-related adverse effects were observed in rats receiving up to 2000 mg d-phenothrin/kg diet for two years. At 6000 mg/kg diet, growth was affected in both sexes. Serum glutamate-pyruvate transferase activity was increased in the males of this dose group.

2.1.7 Supplementary studies of toxicity:

Carcinogenicity: No tumours attributable to d-phenothrin exposure were observed in Swiss mice following 18 months administration of up to 3000 mg/kg diet, or in rats receiving less than 6000 mg/kg diet in the long-term feeding studies described above.

Teratogenicity: No teratogenic effects were observed. The NOELs for New Zealand white rabbits and mice were 30 and 3000 mg/kg b.w./day respectively.

Mutagenicity: Two oral doses of 1500 mg/kg b.w./day to male mice did not induce mutation in a host-mediated assay with *Salmonella typhimurium* -G46. Similar investigations with (1R)-*trans*-phenothrin (250 mg/kg b.w./day) or (1R)-*cis*-phenothrin (90 mg/kg b.w./day) were also negative.

No mutagenic potential was observed with or without metabolic activation of d-phenothrin, or the individual isomers, in several strains of *S. typhimurium* or *Escherichia coli*. d-Phenothrin did not induce mutations in *Bacillus subtilis*. *In vivo* and *in vitro* chromosomal aberration tests showed negative results.

Reproduction: No significant changes in reproductive potential were observed in a three generation reproduction study on Charles River rats. The NOEL was 2000 mg/kg diet.

Neurotoxicity: d-Phenothrin at high doses, in common with pyrethroids of similar chemical structure, may induce ataxia.

Rats receiving oral doses of 5000 mg (1R)-phenothrin/kg b.w./day (as Sumithrin^R) for five days showed evidence of poisoning, such as leg weakness or ataxia, and some died. In survivors three days after cessation of exposure no clinical signs of poisoning were apparent. No significant morphological changes were observed.

Other: (1R) - phenothrin had no effect on a variety of *in vitro* and *in vivo* pharmacological parameters. These tests included hexobarbital sleeping times in mice, body temperature in rats, blood pressure and heart rate in dogs, and the contractile activity of various muscle preparation *in vitro*.

- 2.1.8 **Modifications of toxicity:** The geometric isomers undergo different metabolic pathways (see Section 2.1.3). The rapid hydrolysis of the *trans* - isomers and the slower oxidation of the *cis*-isomers are similar to that observed with other pyrethroids. Inhibition of the oxidative enzymes may increase the toxicity of the *cis* isomers.

2.2 TOXICOLOGY - MAN

- 2.2.1 **Absorption route:** No published data available but d-phenothrin may be absorbed from the skin, gastrointestinal tract or from the lungs.

2.2.2 **Dangerous doses:**

Single: No published information available.

Repeated: No published information available.

- 2.2.3 **Observations on occupationally exposed workers:** No published information available.

- 2.2.4 **Observations on exposure of the general population:** No published information available. Manufacturers' instructions should be carefully followed to ensure that the general population is not exposed to undue amounts of d-phenothrin during agricultural, public health or domestic usage.

- 2.2.5 **Observations on volunteers:** In a special study, d-phenothrin in a talc powder formulation with Span 80 as a stabilizer was applied to the head and pubic hair of eight male volunteers three times at intervals of 3 days, at a dose of 32 mg/man per administration (0.44 to 0.67 mg/kg body weight per day). The powder was washed off 1 hour after application. There were no significant abnormalities due to d-phenothrin in terms of dermal irritation, clinical signs, or blood biochemical and haematological parameters. The blood levels of d-phenothrin were below the detection limit of 0.0006 mg/kg.

- 2.2.6 **Reported mishaps:** No published information available.

2.3 TOXICITY TO NON-MAMMALIAN SPECIES

- 2.3.1 **Fish:** Toxic to fish.

LC₅₀ - 48 hour

Goldfish	0.25 - 0.5 mg/L
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Killifish	0.2 mg/L
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LC₅₀ - 96 hour

Bluegill	0.018 mg/L (1R)-phenothrin
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Rainbow trout	0.017 mg/L (1R)-phenothrin
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- 2.3.2 **Birds:**

LD₅₀ - Oral

Bobwhite quail	> 2510 mg/kg b.w. (1R)-phenothrin
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- 2.3.3 **Other species:** Toxic to bees but no quantitative data are available.

LC₅₀ 3 hour

<i>Daphnia pulex</i>	> 50 mg/L
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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 formulations > 25% - Category 4*

All other formulations - Category 5*

*Based on WHO documented oral LD₅₀ of > 5000 mg/kg b.w.

3.2 TRANSPORTATION AND STORAGE

Formulations in category 4: Should be transported and stored in clearly labelled, leak-proof containers well away from food or drink. The containers should be kept under lock and key, secure from access by children and unauthorized personnel.

Formulations in category 5: Should be transported and stored in clearly labelled, leak-proof containers, well away from food and drink and secure from access by children.

3.3 HANDLING

Formulations in category 4: Protective clothing (see section 4) should be worn when handling these formulations. Adequate washing facilities should be available in the immediate area. Eating, drinking and smoking should be prohibited during handling. Hands and face should be washed immediately after handling the formulation.

Formulations in category 5: Facilities as required for the handling of any chemical should be provided. Hands and face should be washed before eating, drinking or smoking and immediately after handling the compound.

3.4 DISPOSAL AND/OR DECONTAMINATION OF CONTAINERS

Technical d-phenothrin and its formulations (other than pressurized products): Empty containers should be decontaminated (See Section 4.3), but decontaminated containers must not be used for transportation or storage of food or feed stuffs. Containers which are not decontaminated should be burned or crushed and buried below topsoil. Extreme care must be taken to ensure that the disposal site will not cause subsequent contamination of water sources. Pressurized products must be disposed of according to manufacturers' instructions and the containers must never be heated or punctured.

3.5 SELECTION, TRAINING AND MEDICAL SUPERVISION OF WORKERS

Formulations in category 4: Persons under medication with neuroactive drugs should avoid contact with d-phenothrin. Consideration should be given to the workers' ability to comprehend and follow instructions. Workers should be trained in techniques to avoid contact with the formulations.

Formulations in category 5: A warning to workers to avoid contact is essential.

3.6 ADDITIONAL REGULATIONS RECOMMENDED IF DISTRIBUTED BY AIRCRAFT

All formulations: Pilots and loaders should have specialized training in application methods and in the recognition of early symptoms of pesticide poisoning. A suitable respirator should be worn in addition to overalls and impermeable gloves. Flagmen should wear impermeable gloves and boots, overalls and a broad brimmed hat and should be located well away from the dropping zone.

3.7 LABELLING

Formulations in category 4 - Minimum cautionary statement: d-Phenothrin is a synthetic pyrethroid insecticide which may be poisonous following ingestion, skin contact or inhalation of fogs, dusts or mists. These formulations may be irritating to the skin and eyes. Avoid skin contact; wear protective overalls, impermeable gloves and eye protection while handling concentrate. Keep the material out of reach of children and well away from food and feed stuffs. If poisoning occurs call a physician.

Formulations in category 5 - Minimum cautionary statement: This formulation contains phenothrin and is poisonous if swallowed. It may be absorbed from the skin or following inhalation of dusts, mists or fogs. Keep this product out of the reach of children and well away from food and feed stuffs. Wash thoroughly after use.

3.8 RESIDUES IN FOOD

Maximum residue limits have been established by the FAO/WHO Joint Meeting on Pesticide Residues. There are eight Codex Committees MRLs. The Joint FAO/WHO Meeting on Pesticide Residues has estimated the Acceptable Daily Intake (ADI) to be 0.07 mg/kg body weight.

4.0 PREVENTION OF POISONING IN MAN AND EMERGENCY AID

4.1 PRECAUTIONS IN USE

- 4.1.1 **General:** d-Phenothrin is a synthetic pyrethroid which may elicit an effect on nerve function when administered at high doses to animals. It may be absorbed from the gastrointestinal tract or from intact skin. Absorption from the lungs may occur following exposure to dusts, aerosol, mists or fogs formulations.
- 4.1.2 **Manufacture and formulation - TLV:** No published information available. Closed systems and forced ventilation should be used to reduce the exposure of workers to d-phenothrin. Protective clothing (see Section 4.1.3) should be worn.
- 4.1.3 **Mixers and applicators:** Workers should wear impermeable gloves and boots, clean overalls and eye protection. A respirator should additionally be worn during mixing operations and when applying aerosol, mist, dust or fog formulations. Mixing, if not mechanical, should always be carried out with a paddle of appropriate length. Avoid contact with the mouth, skin and eyes. Before eating, drinking, or smoking, the face, hands and exposed skin should be thoroughly washed.
- 4.1.4 **Other associated workers:** Persons associated with the application of d-phenothrin should observe the precautions described above (see sections 3.6 and 4.1.3).
- 4.1.5 **Other populations likely to be affected:** The domestic and public health usage of d-phenothrin will expose persons other than those associated with agricultural practices. Careful attention to the manufacturers' instructions and the low concentrations of d-phenothrin in many formulations should ensure that this usage dose not expose the public to hazardous amounts of d-phenothrin.

Good agricultural practices should ensure that the general public are not exposed to hazardous amounts of d-phenothrin following commercial applications.

4.2 ENTRY OF PERSONS INTO TREATMENT AREA

Entry of unprotected persons into enclosed areas treated with aerosol, mist or fog formulations should be prevented until the area has been thoroughly ventilated.

4.3 DECONTAMINATION OF SPILLAGE AND CONTAINERS

Care must be taken during decontamination procedures to ensure that water sources are not contaminated. Impermeable gloves and eye protection should be worn. Residues in containers should be emptied in a diluted form into a dry pit deeper than 0.5 m. Dispose of pressurized products according to manufacturers' recommendations. These containers should not be punctured, heated or burned. For other products, the empty container may be decontaminated by scrubbing with water and detergent followed by soaking overnight with 5% sodium hydroxide solution. Decontaminated containers must not be used for the transportation or storage of food or drink. Containers which are not decontaminated should be burned or crushed and buried below topsoil.

Spillage of liquid formulations should be covered with absorbent material. This material, or spillage of dry formulations, should be collected and burned or buried in a deep dry pit. Residual contamination should be removed from the spillage site by washing with water and detergent.

4.4 EMERGENCY AID

4.4.1 Early symptoms of poisoning: No reported incidences. Unless exposure to d-phenothrin has been exceptionally high, the symptoms of over-exposure may be due to the accompanying chemicals in the formulation. Symptoms may include headache, nausea and vomiting.

4.4.2 Treatment before person is seen by physician, if these symptoms appear following exposure: The person should stop work immediately, remove contaminated clothing and wash the affected skin area. If the formulation has entered the eyes they should be flushed with clean water. The majority of formulations contain hydrocarbon solvents or oils. Vomiting should not be induced unless it can be definitely determined that all of the following apply: that the formulation was free of solvents and oil; that large amounts of the formulation have been ingested; that the patient is fully conscious. In all cases, keep the patient calm and obtain immediate medical help.

5.0 FOR MEDICAL AND LABORATORY PERSONNEL

5.1 MEDICAL DIAGNOSIS AND TREATMENT IN CASES OF POISONING

5.1.1 General information: d-Phenothrin is a synthetic pyrethroid insecticide of low mammalian toxicity. It may be absorbed from the gastrointestinal tract; by inhalation of dusts, mists or fogs or through intact skin. d-Phenothrin is rapidly metabolized to hydrolysis and oxidation products, which are rapidly excreted in the urine and faeces.

5.1.2 Symptoms and signs: No published information available on the acute toxic effects of d-phenothrin in humans. Accompanying chemicals in the formulation may elicit symptoms before those observed from d-phenothrin exposure. Early symptoms may include headache, nausea and vomiting.

5.1.3 Laboratory: There are no simple methods for determining d-phenothrin in body fluids. The metabolism is rapid and there are numerous excretory products. The proportion of each metabolite may not be constant in all types of exposure and cannot therefore be used as a quantitative measure of exposure. Some urinary metabolites may not be specific to d-phenothrin.

- 5.1.4 **Treatment:** Treatment is symptomatic. Wash contaminated skin with soap and water. Wash contaminated eyes with copious amounts of water. Ingestion of a small amount (< 5 mg/kg b.w.) of d-phenothrin should be treated with a large dose of activated charcoal followed by sodium or magnesium sulfate (0.25 g/kg b.w.) in water.

Following ingestion of larger quantities of d-phenothrin, vomiting should be induced if the patient is fully conscious. Care must be taken however to avoid pulmonary complications from the accompanying solvents or oils. Subsequent administration of activated charcoal may limit absorption of remaining d-phenothrin.

- 5.1.5 **Prognosis:** There are no published data available. Based on animal experiments it is expected that any effects should be reversible.

- 5.1.6 **References to previously reported cases:** No published information available.

- 5.2 **SURVEILLANCE TESTS** - None.

- 5.3 **LABORATORY METHODS**

- 5.3.1 **Detection and assay of compound and residues:**

Papadopoulou-Mourkidou E, Iwata Y, Gunther FA (1984), J Agric Food Chem 32: 800-805.

Sakaue S, Kitajima M, Horiba M, Yamamoto S (1981), Agric Biol Chem 45(5): 1135-1140.

- 5.3.2 **Other tests in case of poisoning:** None.

REFERENCES

1. WHO (1990), Environmental Health Criteria 96; d-Phenothrin; Geneva, World Health Organization, 64 pp.
2. WHO (1989), Health and Safety Guide 32; d-Phenothrin; Geneva, World Health Organization, 28 pp.
3. FAO/WHO (1980) Pesticide Residues in Food 1988, Evaluations 1988, Part II - Toxicology, FAO Plant Production and Protection Paper 93/2, Rome, 1989.
4. The Pesticide Manual, A World Compendium (9th edition 1991), Worthing, C.R. and Hance, eds., British Crop Protection Council, 20 Bridport Road, Thornton Heath, CR4 7QG, United Kingdom.
5. WHO (1991), Fourteenth Report of the WHO Expert Committee on Vector Biology and Control, WHO Technical Report Series No. 813, Safe Use of Pesticides; Geneva, World Health Organization, 27 pp.

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