### **Phorate**

### Guideline

The maximum acceptable concentration (MAC) for phorate in drinking water is 0.002 mg/L (2 µg/L).

## Identity, Use and Sources in the Environment

Phorate ( $C_7H_{17}O_2PS_3$ ) is an organophosphorous insecticide and acaricide used for the control of sucking and biting insects, mites and certain nematodes on root and feed crops, cotton, brassicas and coffee. Between 50 000 and 100 000 kg are used annually in Canada. Phorate has a vapour pressure of 0.11 Pa at 20°C; its solubility in water at 25°C is 50 mg/L. Reported log octanol—water partition coefficients range from 2.92 to 4.26.3

Phorate released to the soil is rapidly oxidized to the sulphoxide and sulphone forms and their phosphorothioate analogues, which are then hydrolysed.<sup>4</sup> Phorate sulphoxide and sulphone are generally more persistent than the parent compound.<sup>5</sup> Phorate has some potential to leach through the soil to groundwater.<sup>5</sup> Its half-life in aqueous solution at pH 8 and 70°C is two hours.<sup>6</sup>

### **Exposure**

Phorate was not detected in 24 samples of municipal and private drinking water supplies in two cities (Harrow, 1985, and Toronto, 1971 to 1982) in Ontario (detection limit  $0.02~\mu g/L$ ). It was found in one of seven samples from Prince Edward Island at a level of  $150~\mu g/L$  (date and detection limit not reported).<sup>7</sup> It was not detected in 949 stream water samples from 11 agricultural watersheds in southern Ontario from 1975 to 1977 (detection limit not reported)<sup>8</sup> or in 446 samples from three Ontario river basins surveyed from 1981 to 1985 in which more than 1200~kg of phorate were applied annually (detection limit  $0.1~\mu g/L$ ).<sup>9</sup>

Based on the residue tolerance limits established by the Food Directorate of the Department of National Health and Welfare, <sup>10</sup> the theoretical maximum daily intake of phorate from food is 0.026 mg. The actual average daily intake for a 70-kg adult is estimated to be  $0.21 \mu g$ , based on a U.S. market basket survey.<sup>11</sup>

# **Analytical Methods and Treatment Technology**

The content of phorate in water may be determined by extracting into dichloromethane, drying the extract and redissolving it in hexane and analysing by gas–liquid chromatography with flame photometric detection (detection limit 0.1 µg/L).<sup>9</sup>

No information on the effectiveness of current treatment technology in removing phorate from drinking water was identified.

### **Health Effects**

Phorate is readily absorbed from the gastrointestinal tract. It is metabolized in animals to phorate sulphoxide and sulphone and their phosphorothioate analogues, followed by hydrolysis to dithio-, thio- and orthophosphoric acids. Thirty-five percent of an orally administered dose of 2 mg/kg bw of radioactively labelled phorate was eliminated in the urine and 3.5% in the faeces of rats within six days. Metabolites found in the urine of phorate formulators include diethyl phosphate, diethyl phosphorothioate and diethyl thiophosphate.

Phorate is reported to be one of the more toxic cholinesterase-inhibiting organophosphorous insecticides.<sup>5</sup> In occupationally exposed workers, there was a significant depression in the level of plasma cholinesterase activity to 46 and 29% of normal levels after one and two weeks of exposure, respectively. Recovery of up to 79% of normal activity was reported 10 days after exposure was ceased. Whole blood cholinesterase levels were depressed to 90 and 86% of normal after one and two weeks of exposure. Neurological (headache, giddiness, fatigue) effects, gastrointestinal (nausea, vomiting, stomachache) effects, skin and eye irritation and lowering of heart rate were among the symptoms reported.<sup>14</sup>

Groups of three dogs (two females and one male) were administered phorate in encapsulated corn oil in doses of 0, 0.01, 0.05, 0.25 or 1.25 mg/kg bw per day six days per week for 15 weeks. In animals receiving 0.05 mg/kg bw per day, there was a significant decrease in plasma cholinesterase activity; higher exposure levels produced significant depressions in both plasma and red cell cholinesterase activity. The no-observed-adverse-effect level (NOAEL) was considered to be 0.01 mg/kg bw per day, although a slight decrease in plasma cholinesterase was observed at this level.<sup>15</sup>

Groups of 50 male and 50 female CRL:COBS CD(SD)BR rats were fed diets containing phorate at levels of 0, 1, 3 or 6 ppm (approximately equivalent to doses of 0, 0.05, 0.15 and 0.30 mg/kg bw per day, respectively) for two years. A significant decrease in plasma cholinesterase activity was observed in males exposed to 0.30 mg/kg bw per day at 12 months, in males of all dose groups at 24 months and in females consuming 0.15 and 0.30 mg/kg bw per day at 3, 6, 12 and 24 months. Erythrocyte cholinesterase activity was not significantly depressed. Brain cholinesterase activity was significantly depressed in males at 0.30 mg/kg bw per day and in females at 0.15 mg/kg bw per day and above. There was no significant difference in the incidence, type and time of detection of tumours between the control group and the treated animals. The NOAEL for rats for plasma and brain cholinesterase inhibition in this study was considered by the authors to be 0.05 mg/kg bw per day. 16

Teratological studies were conducted on groups of 25 mated female rats (CRL:COBS CD(SD)BR strain) administered doses of phorate of 0, 0.125, 0.25 or 0.50 mg/kg bw per day by intubation on gestation days 6 through 15. There was an increased incidence of enlarged hearts in foetuses whose dams had been exposed to 0.5 mg/kg bw per day. No other significant differences between the exposed and control groups were noted. The NOAEL for teratogenic effects was considered by the researchers to be 0.25 mg/kg bw per day. <sup>17</sup>

Phorate was not found to be mutagenic in bacterial systems, <sup>18</sup> nor did it produce any dominant lethal mutations in mice. <sup>19</sup>

#### **Rationale**

The acceptable daily intake (ADI) of phorate has been established by the Food and Agriculture Organization (FAO) and the World Health Organization (WHO)<sup>20</sup> as 0.0002 mg/kg bw per day, based on the NOAELs of 0.01 mg/kg bw per day in dogs<sup>15</sup> and 0.05 mg/kg bw per day in rats.<sup>16</sup>

The maximum acceptable concentration (MAC) for phorate in drinking water is therefore derived as follows:

MAC = 
$$\frac{0.0002 \text{ mg/kg bw per day} \times 70 \text{ kg bw} \times 0.20}{1.5 \text{ L/d}} \approx 0.002 \text{ mg/L}$$

#### where:

- 0.0002 mg/kg bw per day is the ADI established by the FAO/WHO
- 70 kg bw is the average body weight of an adult
- 0.20 is the proportion of daily intake of phorate allocated to drinking water
- 1.5 L/d is the average daily consumption of drinking water by an adult.

### References

- 1. Environment Canada/Agriculture Canada. Pesticide registrant survey, 1986 report. Commercial Chemicals Branch, Conservation and Protection, Environment Canada, Ottawa (1987).
- 2. Hayes, W.J., Jr. Pesticides studied in man. Williams and Wilkins, Baltimore, MD (1982).
- 3. Suntio, L.R., Shiu, W.Y., Mackay, D., Seiber, J.N. and Glotfelty, D. Critical review of Henry's law constants for pesticides. Rev. Environ. Contam. Toxicol., 103: 1 (1988).
- 4. The Royal Society of Chemistry. The agrochemicals handbook. 2nd edition. Update 1—April 1988. Nottingham, England (1988).
- Hazardous Substances Data Base. Toxicology Data Network,
  U.S. National Library of Medicine, Bethesda, MD (1988).
- National Academy of Sciences. Drinking water and health.
  Vol. I. National Research Council, Washington, DC (1977).
- Hiebsch, S.C. The occurrence of thirty-five pesticides in Canadian drinking water and surface water. Unpublished report prepared for the Environmental Health Directorate, Department of National Health and Welfare (1988).
- 8. Braun, H.E. and Frank, R. Organochlorine and organophosphorus insecticides: Their use in eleven agricultural watersheds and their loss to stream waters in Southern Ontario, Canada, 1975–1977. Sci. Total Environ., 15: 169 (1980).
- 9. Frank, R. and Logan, L. Pesticide and industrial chemical residues at the mouth of the Grand, Saugeen and Thames rivers, Ontario, Canada, 1981–85. Arch. Environ. Contam. Toxicol., 17: 741 (1988).
- 10. Department of National Health and Welfare. National pesticide residue limits in foods. Food Directorate, Ottawa (1986).
- 11. Gartrell, M.J., Craun, J.C., Podrebarac, D.S. and Gunderson, E.L. Pesticides, selected elements, and other chemicals in adult total diet samples, October 1980–March 1982. J. Assoc. Off. Anal. Chem., 69(1): 146 (1986).
- 12. FAO/WHO. Pesticide residues in food—1977. Evaluations. Data and recommendations of the Joint Meeting on Pesticide Residues, Geneva, 6–15 December 1977. FAO Plant Production and Protection Paper No. 10 (Suppl.), Food and Agriculture Organization of the United Nations, Rome (1978).
- 13. Brokopp, C.D., Wyatt, J.L. and Gabica, J. Dialkyl phosphates in urine samples from pesticide formulators exposed to disulfoton and phorate. Bull. Environ. Contam. Toxicol., 26: 524 (1981).
- 14. Kashyap, S.K., Jani, J.P., Saiyed, H.N. and Gupta, S.K. Clinical effects and cholinesterase activity changes in workers exposed to phorate (Thimet). J. Environ. Sci. Health, B19(4–5): 479 (1984).

- 15. Tusing, T.W. 13-week subacute Thimet feeding study in male and female rats. Unpublished report of the American Cyanamid Co. (1956), cited in reference 6.
- 16. Litton Bionetics, Inc. 24-month chronic toxicity and potential carcinogenicity study in rats. Phorate. Unpublished final report from Litton Bionetics, Inc., submitted to the World Health Organization by American Cyanamid Co. (1981). Cited in FAO/WHO. Pesticide residues in food—1982. Evaluations. Data and recommendations of the Joint Meeting on Pesticide Residues, Rome, 23 November—2 December 1982. FAO Plant Production and Protection Paper No. 49, Food and Agriculture Organization of the United Nations, Rome (1983).
- 17. Litton Bionetics, Inc. Teratology study in rats. Thimet<sup>R</sup> phorate. Unpublished final report from Litton Bionetics, Inc., submitted to the World Health Organization by American Cyanamid Co. (1978). Cited in FAO/WHO. Pesticide residues in food—1982. Evaluations. Data and recommendations of the Joint Meeting on Pesticide Residues, Rome, 23 November–2 December 1982. FAO Plant Production and Protection Paper No. 49, Food and Agriculture Organization of the United Nations, Rome (1983).
- 18. Simmon, V.F., Poole, D.C. and Newell, G.W. In vitro mutagenic studies of twenty pesticides. Toxicol. Appl. Pharmacol., 37: 109 (1976), cited in reference 2.
- 19. Jorgenson, T.A., Rushbrook, C.J. and Newell, G.W. *In vivo* mutagenesis investigations of ten commercial pesticides. Toxicol. Appl. Pharmacol., 37: 109 (1976), cited in reference 2.
- 20. WHO/FAO. Pesticide residues in food—1985. Evaluations. Joint Meeting on Pesticide Residues, Geneva, 23 September–2 October 1985. FAO Plant Production and Protection Paper No. 72/1, Food and Agriculture Organization of the United Nations, Rome (1986).