



# ChemicalWatch Factsheet

A Beyond Pesticides/ NCAMP Factsheet

## Thiram

Among the most hazardous pesticides, the fungicides thiram, ziram and ferbam are teratogens, neuro, reproductive and thyroid toxins, mutagens, and skin sensitizers. Ziram is also a carcinogen, indicting thiram and ferbam, as these fungicides are closely related and have a common mechanism of toxicity.<sup>1,2,3,4</sup>

Thiram, tetramethylthiuram disulfide, is used extensively as an agricultural fungicide, seed protectant and animal repellent, and contaminates the environment as a degradation product of the widely used fungicides – ziram and ferbam. Thiram is also an ingredient in certain medicated soaps and suntan and antiseptic sprays.<sup>6</sup> First produced in 1931 by Dupont, thiram is now made by Gustafson, Prochimie International and others.<sup>6,7</sup> Many workers are exposed to the dithiocarbamates in the rubber and plastic industries, where the dithiocarbamates are used as preservatives.

The pesticides degrade to a variety of toxic products, including the potent neurotoxins carbon disulfide and dimethyldithiocarbamate, a cholinesterase inhibitor, and dimethylamine, a possible carcinogenic nitrosamine.<sup>5,8,9,10</sup> On heating they form ethylene thiourea, a thyroid toxin and carcinogen.<sup>11</sup>

Contact dermatitis is among the most important human toxic effects of these fungicides. Exposure to one can result in sensitivity to related pesticides and to a wide variety of rubber products in which these fungicides are used as preservatives, such as gloves, mattresses, goggles, diaphragms and condoms.<sup>12</sup> Sym-

tract.<sup>5</sup> The thyroid was the primary target organ with enlargement, carcinoma and other abnormalities in manufacturing workers.<sup>14</sup> Prolonged occupational exposure caused tearing, sensitivity to light and reduced vision.<sup>5</sup> Dithiocarbamates also interfere with metabolism of toxins by

inhibiting liver microsomal enzymes, thereby causing a potential synergistic reaction with other pesticides.<sup>15</sup>

Acute oral toxicity resulted in ulceration of the gastrointestinal tract, necrosis of the liver and renal tubules and demyelination in the brain.<sup>1</sup> Con-

tact dermatitis of the allergic type was observed in rabbits after administration of thiram into skin.<sup>5</sup>

Thiram is severely teratogenic in mice, hamsters and chicks.<sup>16,17,18,19</sup> The various defects in mice and hamsters included exencephaly, cleft palate, limb anomalies, and fused lumbar and sacral vertebrae. Birth defects in chicks included total or partial absence of lids and cornea of the eye, encephalocele (absence of top of skull with bulging brain), wing and shoulder abnormalities and defects of the chest wall. The

### *chemicalWATCH* Stats:

**CAS Registry Number:** 137-26-8

**Chemical Class:** Dithiocarbamate

**Use:** Fungicide on food crops (strawberries, apples, and peaches) and for seed treatment

**Toxicity rating:** Slightly toxic

**Signal Word:** Caution

**Health Effects:** Neurotoxic; developmental and reproductive toxicity

**Environmental Effects:** Moderately to very highly toxic to freshwater, estuarine and marine organisms. May reach surface waters in concentrations high enough to affect aquatic life.

ptoms include: irritation of the mucous membranes, conjunctivitis, rhinitis, sneezing and coughing. Moisture and sweat can leach the chemicals out of the rubber, while fats and oils facilitate absorption.<sup>13</sup>

Symptoms of acute human poisoning include: nausea, vomiting, diarrhea, headache, lethargy, dizziness, ataxia, confusion, drowsiness, flaccid paralysis and death. Prolonged occupational exposure to thiram increased the incidence of hypertension and diseases of the heart, liver, thyroid and gastrointestinal

dithiocarbamates are also extremely embryotoxic substances with lethality, as well as malformations, at very low doses in eggs.<sup>18</sup> Pre- and post-implantation embryotoxic and teratogenic effects were observed in ziram treated rats.<sup>20</sup>

Dithiocarbamate pesticides have a marked spermicidal activity in humans.<sup>21,22</sup> They also cause viable and non-viable gross morphological alterations of sperm.<sup>22</sup> In animals, dithiocarbamate pesticides given to young and adult domestic chickens produced retarded testicular development and atrophy,<sup>23</sup> and ziram induced atrophy of the testes in both mice and rats.<sup>2,24</sup> Decreased egg production and ovarian and oviduct atrophy were observed in bobwhite quail.<sup>25,26</sup> Chronic thiram exposure has caused abortion in pregnant animals.<sup>5</sup>

Thiram neurotoxicity is characterized by depression, disturbances

in coordination and convulsions.<sup>11</sup> Rats given thiram developed ataxia and paralysis of the hind legs, demyelination and degeneration in the sciatic nerve and spinal cord, and behavioral changes and hyperactivity.<sup>27</sup> Epileptic seizures developed in dogs fed ziram.<sup>2</sup>

Ziram causes thyroid cancer in rats and lung and lymph gland cancer in mice.<sup>14</sup> Chicks became lame and their "long bones developed greatly swollen epiphyses." The histological description indicates that these lesions were probably bone neoplasms. Similar epiphyseal alterations of the tibia and femur were observed in rats given ziram.<sup>28</sup>

Thiram causes mutagenic effects in mice characterized by chromosomal aberrations in bone marrow cells.<sup>29</sup> Ziram is mutagenic in numerous studies in a wide variety of tests.<sup>11</sup>

Most tolerances for thiram are 7

ppm.<sup>30</sup> EPA notes that insufficient data are available to assess the adequacy of these tolerances.

Thiram is very highly toxic to both cold water and warm water fish.<sup>30</sup> The pesticide is moderately toxic to birds. Generally the subcutaneous toxicity to mammals is high. The LD50 for pheasants was 485 to 932 mg/kg.<sup>5</sup>

In fish fed radioactively labeled ziram, high levels of ziram were observed in the eye, skin, kidney, thyroid, liver, gall bladder and intestinal lumens.<sup>31</sup> After 16 days, 45% of the compound was present in the body.

#### **Update, November 2007:**

In September 2004 by signing the Reregistration Eligibility Decision (RED) for thiram. Thiram is of low to moderate acute toxicity (Toxicity Category III) via oral and dermal routes of exposure and is moderately toxic (Toxicity Category II) for dermal irritation and inhalation hazards. It is a moderate skin sensitizer. Thiram is listed as an endocrine disruptor on the Colborn list, as well as in the European Union.

Although the environmental fate database for thiram is incomplete, there are numerous environmental effects associated with thiram exposure. In the RED, EPA says that thiram is sufficiently mobile and persistent that it could reach surface waters at concentrations high enough to affect aquatic life.

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## Thiram *chemicalWATCH* Factsheet Bibliography

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- <sup>1</sup> Gosselin, R.E., R.P. Smith and H.C. Hodge. 1984. Clinical toxicology of commercial products. Fifth ed., Williams & Wilkins, Baltimore, MD.
- <sup>2</sup> Hodge, H.C., E.A. Maynard, W.L. Downs, R.D. Coye L.T. and Steadman. 1956. Chronic oral toxicity of ferric dimethyldithiocarbamate (ferbam) and zinc dimethyldithiocarbamate (ziram). J. Pharmacol. Exp. Ther. 118:174-81.
- <sup>3</sup> Lee, C.C., J.Q. Russell and J.L. Minor. 1978. Oral toxicity of ferric dimethyldithiocarbamate (ferbam) and tetramethylthiuram disulfide (thiram) in rodents. J. Toxicol. Environ. Hlth. 4:93-106.
- <sup>4</sup> Hodgson, J.R. C.C. and Lee. 1977. Cytotoxicity studies on dithiocarbamate fungicides. Toxicol. Appl. Pharmacol. 40:19-22.
- <sup>5</sup> Dalvi, R.R. 1988. Toxicology of thiram (tetramethylthiuramdisulfide): a review. Veter. Hum. Toxicol. 30:480-2.
- <sup>6</sup> Thomson, W.T., 1985. Agricultural Chemicals Book IV - Fungicides. Thomson Publications, Fresno, CA.
- <sup>7</sup> Farm Chemicals Handbook '92. Meister Publishing Company, Willoughby, OH.
- <sup>8</sup> Dalvi, R.R. and Deoras, D.P. 1986. Metabolism of a dithiocarbamate fungicide thiram to carbon disulfide in the rat and its hepatotoxic implications. Acta. Pharmacol. Toxicol. 58:38-42.
- <sup>9</sup> Nietsche, I., et al. 1975. Studies on the metabolism of dialkyldithiocarbamates. In: Proc. Third Intern. IUPAC Congo. George Thieme Publishers, Stuttgart, pp. 292-7.
- <sup>10</sup> International Agency for Research on Cancer. 1976. Some carbamates, thiocarbamates and carbazides. IARC Monogr. Eval. Careinog. Risk Chem. Man. 12. World Health Organization, IARC, p. 259-70.
- <sup>11</sup> Fishbein, L. 1976. Environmental health aspects of fungicides. I. Dithiocarbamates. J. Toxicol. Environ. Health 1:713-35.
- <sup>12</sup> Shelly, W.B. 1964. Golf course dermatitis due to thiram fungicide. Cross hazards of alcohol, disulfiram and rubber. JAMA 188:415-17.
- <sup>13</sup> Council on Pharmacy and Chemistry, AMA. 1955. Outlines on information on pesticides. JAMA 157:237-41.
- <sup>14</sup> National Toxicology Program. 1983. Carcinogenesis bioassay of ziram in F344/N rats and B6C3F1 mice (feed study). Technical Report Series No. 238.
- <sup>15</sup> Dalvi, R.R., et al. 1984. Thiram induced toxic liver injury in male Sprague Dawley rats. J. Environ. Sci. Health B19:703-12.
- <sup>16</sup> Matthiaschk, G. 1973. Uber den einfluss von L-cystein auf der teratogenese durch thiram (TMTD), bei NMRI-mausen. Arch. Toxicol. 30:251-62.
- <sup>17</sup> Robens, J.P. 1969. Teratogenic studies on carbaryl, diazinon, norea, disulfiram and thiram in small laboratory animals. Toxicol. Appl. Pharmacol. 15:152-63.

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## Thiram *chemicalWATCH* Factsheet Bibliography

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- <sup>18</sup> Korhonen, A., K. Hemminki and H. Vainio. 1983. Embryotoxicity of industrial chemicals on the chicken embryo: dithiocarbamates. *Terato. Carcino. Mutagen.* 3:163-75.
- <sup>19</sup> Roll, R. 1971. Teratologische untersuchungen mit thiram (TMT) an zwei mausestammer. *Arch. Toxikol.* 27:173-86.
- <sup>20</sup> Giavini, E., C. Vismara and M.L. Broccia. 1983. Pre- and post-implantation embryotoxic effects of zinc dimethyldithiocarbamate (ziram) in the rat. *Ecotoxicol. Environ. Safety* 7:531-7.
- <sup>21</sup> Holzaepfel, J.W., R.P. Greenlee and R.E. Wyant. 1959. *Fertil. Steril.* 10:272.
- <sup>22</sup> Rice, E.W. 1964. Morphological changes in human spermatozoa following treatment of semen with certain dialkyldithiocarbamates. *Exper. Cell Res.* 34:186-8.
- <sup>23</sup> Raasul, A.R. and J.McC. Howell. 1974. The toxicity of some dithiocarbamate compounds in young and adult domestic fowl. *Toxicol. Appl. Pharmacol.* 30:63-78.
- <sup>24</sup> Cilievici, O., C. Craciun and E. Ghidus. 1983. Decreased fertility, increased dominant lethals, skeletal malformations induced in the mouse by ziram fungicide. *Morphol. Embryol. Buecares* 29:159-65.
- <sup>25</sup> Wedig, J., A. Cowan and R. Hartung. 1968. Some of the effects of tetramethylthiuramdisulfide (TMTD) on reproduction of the bobwhite quail. *Toxicol. Appl. Pharmacol.* 12:293-7.
- <sup>26</sup> Clarke, E.C.G. and M. Clarke. 1975. *Veterinary Toxicology.* Williams and Wilkins, Baltimore, MD. pp. 182-4.
- <sup>27</sup> Lee, C.C. and P.J. Peters. 1976. Neurotoxicity and behavioral effects of thiram in rats. *Environ. Health Perspect.* 17:35-43.
- <sup>28</sup> Enomoto, A., T. Harada, K. Maita, and Y. Shirasu. 1989. Epiphyseal lesions of the femur and tibia in rats following oral chronic administration of zinc dimethyldithiocarbamate (ziram). *Toxicol.* 54:45-58.
- <sup>29</sup> Kurinnyi, A.I. and T.I. Kendratenko. 1972. Effect of fungicides (dithiocarbamic acid) derivation on chromosomes of bone marrow cells in mice. *Tsitol. Genet.* 6:225-8 (quoted by Dalvi, 1988).
- <sup>30</sup> EPA. 1984. Pesticide Fact Sheet: Thiram. June 1.
- <sup>31</sup> Van Leeuwen, et al. 1986. Uptake, distribution and retention of zineb and ziram in rainbow trout (*Salmo Gairdner*). *Toxicol.* 42:33-46.
- <sup>32</sup> EPA. 2004. Reregistration Eligibility Decision for Thiram. Office of Pesticide Programs. Washington, DC.