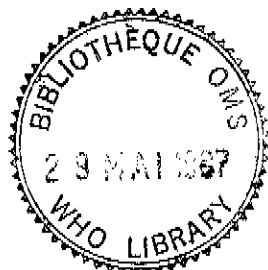


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DATA SHEET ON PESTICIDES

No. 73

ZIRAM



CLASSIFICATION:

Primary Use: Fungicide

Secondary Use: Animal repellent

Chemical Group: Dithiocarbamate

1.0 GENERAL INFORMATION

1.1 COMMON NAME: Ziram (ISO, BSI and JMAF; exception West Germany)

1.1.1 Identity:

IUPAC: Zinc dimethyldithiocarbamate

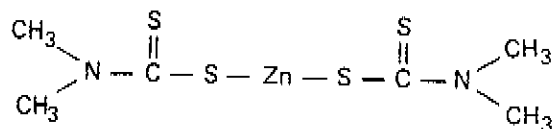
CAS: (T-4)-bis (dimethyldithiocarbamate) zinc

CAS Reg. No.: 137-30-4

Molecular formula: $C_6H_{12}N_2S_4Zn$

Molecular weight: 305.8

Structural formula:



1.1.2 Synonyms - Aaproct^R; Aavolet^R; Aazira^R; Accelerator LR; Aceto ZDED^R; Aceto ZDMR^R; Alcobra ZM^R; Carbazinc^R; Corona Corozate^R; Corozate^R; Cuman^R; Cymate^R; Drupina 90^R; Eptac 1^R; ENT 988; Fulcasin (Fuklasin)^R; Fungostop^R; Hermat ZDM^R; Hexazir^R; Karbam White^R; Methasan^R; Methazate^R; Methylzimate; Methylzineb; Methylziram; Mexene (apezene)^R; Miblam (capilban)^R; Molurame^R; Mycronil^R; NCI-C50442; Pomarsol Z forte^R; Prodaram^R; Rhodiacid^R; Soxinal (Soxinol) PZ^R; Tricarbamix Z; Triscabol^R; Tsimat^R; Tsimat; USAF P-2; Vancide MZ-96^R; Vulcacure^R; Vulkacite (Vulkacit)LR; Weissstaub; Z 75^R; Zarlate; ZC (Z-C) spray^R; Zerlate^R; Zimate^R; Zincmate^R; Zinkcarbamate^R; Zirame; Ziramvis^R; Zirasan^R; Zirbeck^R; Zirex; Ziride^R; Zirthane^R; Zitox^R.

1.2 SYNOPSIS: Ziram is a dithiocarbamate fungicide with some insect repellent properties. It is a metabolic poison of low acute toxicity to mammals: it may cause skin irritation. It is listed in WHO Hazard Class III. Ziram is toxic to zinc sensitive plants. It has also been used extensively in the rubber industry as a promoter of vulcanization.

1.3 SELECTED PROPERTIES

1.3.1 Physical characteristics - Ziram is a colourless odourless powder which melts at 250°C, the technical product melts at 240-244°C. It is corrosive to copper and iron.

1.3.2 Solubility - In water, 65 mg/l at 25°C; it is slightly soluble in ethanol and diethyl ether, moderately soluble in acetone, and soluble in dilute alkali, chloroform and carbon disulphide.

1.3.3 Stability - Ziram is stable under normal conditions but decomposes in acid media. It does not accumulate in soil.

1.3.4 Vapour pressure - Negligible at room temperature.

1.4 AGRICULTURE, HORTICULTURE AND FORESTRY

1.4.1 Common formulations - These include a wettable powder, 300-960 g a.i./kg; a repellent paste; 370 g a.i./kg with sticker; dusts, 35-75 g a.i./kg; and a flowable formulation, 479 g a.i./l.

1.4.2 Pests controlled - It may be used as a repellent against Japanese beetles and cucumber beetles and as a fungicide in the control of several plant diseases. Aquatic snails may also be controlled effectively.

1.4.3 Use pattern - Ziram is used on almonds, apples, apricots, bananas, beans, beets, blueberries, broccoli, brussel sprouts, cabbage, caneberrries, cauliflower, carrots, cantaloupes, celery, cherries, collards, cranberries, cucumbers, melons, nectarines, onions, peaches, pears, pecans, peppers, pumpkins, radishes, squash, spinach, strawberries, tomatoes, turnips, watermelons and ornamentals. It may be applied at 3-16 kg/ha up to the day of harvest on some crops. It is compatible with common fungicides and pesticides except those containing copper or mercury. If plants are difficult to wet, a sticker may be added to the formulation.

1.4.4 Unintended effects - Ziram is non-phytotoxic except to zinc sensitive crops such as Tobacco and cucurbits at high application rates. It is not known to be repellent to beneficial insects.

1.5 PUBLIC HEALTH PROGRAMMES - There are no recommended uses.

1.6 HOUSEHOLD USE - There are no recommended uses.

2.0 TOXICOLOGY AND RISKS

2.1 TOXICOLOGY - MAMMALS

2.1.1 Absorption route - Ziram is slowly absorbed from the gastrointestinal tract; through the intact skin; and by inhalation of spray mist and dusts.

2.1.2 Mode of action - Ziram and other dithiocarbamates are metabolic poisons. Their acute toxic effects are similar to those of carbon disulfide which has led to the suggestion that this metabolite, common to all dithiocarbamates, is the cause of their effects. This is supported by the observation that most dithiocarbamates of very low acute toxicity are excreted unmetabolized in the feces following oral dosing. The exact mode of action is unknown. However, microsomal injury and cytochrome P-450 injury accompanied by increased heme-oxygenase activity is a common occurrence with these compounds. Monoamine oxidase inhibition, abnormal Vitamin B₆ and tryptophane metabolism and cellular loss of zinc and copper have been implicated in studies of the biochemical effect. Ziram is not a potent initiator of thyroid dysfunction among dithiocarbamates and the effects have not been shown to be dose dependent. The metabolically generated sulfur inhibits some intracellular enzyme systems.

2.1.3 Excretion products - Although the metabolism and excretion of ziram has not been extensively studied, insight can be gained from pooled information from other dithiocarbamate studies. Initial degradation probably occurs in the gastrointestinal tract where the parent compound is reduced to the carbamic acid residue which is rapidly absorbed and metabolized by hepatic enzymes. A portion of the acid may be excreted, unchanged, as a glucuronide. Further metabolism of the acid releases CS₂ and dimethylamine. A high proportion of the parent compound may be metabolized to carbon disulfide and the small portion recovered in blood or in expired air represents only that portion of the dose not involved in tissue reactions. Dimethyldithiocarbamate may also be degraded to dimethylthiocarbamate, sulfate and formaldehyde following methylation and oxidation reactions in body tissues in general. Dimethylthiocarbamic acid is excreted as a glucuronide.

2.1.4 Toxicity, single dose -

Dermal LD₅₀: No information.

Oral LD₅₀:

Rat (F)	1400 mg/kg b.w.
Mouse	480 mg/kg b.w.
Rabbit	400 mg/kg b.w.

I.P. LD₅₀:

Rat (M,F)	23 mg/kg b.w.
Mouse	73 mg/kg b.w.

I.V. LD₅₀:

Mouse	18 mg/kg b.w.
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2.1.5 Toxicity, repeated dose - No mortality or growth retardation in weanling rats followed oral daily doses of 100 mg/kg b.w. for one month. Normal thyroid tissues were found in rats ingesting diets containing 0.25% of ziram for one month.

2.1.6 Dietary studies -

Short term: Rats survived dietary levels of 5000 and 2500 mg/kg diet for a month but growth was retarded and there was slight anaemia. Growth retardation at 500 mg/kg diet was slight.

Convulsions occurred in dogs fed ziram at a rate of 25 mg/kg b.w./day and some died after five to nine months. Symptomatology, haematology, urinalysis, organ weights and histology were normal in dogs fed 5.0 or 0.5 mg/kg b.w./day for one year.

Ziram administered in the diet of female rats at 2.5 mg/kg b.w. for nine months resulted in decreased antibody formation, phagocytic activity and complement activity. Lymphatic blastogenic centres in spleen were also reduced.

Long term: Rats were fed ziram 0, 25, 250 or 2500 mg/kg of diet for two years. Rats fed 2500 mg/kg suffered retarded growth and rats fed 250 mg/kg developed atrophic testes.

- 2.1.7 Carcinogenicity: The limited data available does not permit adequate assessment of the carcinogenic potential of ziram. In the feeding study above, 11 tumours were found in treated rats, three malignant tumours of pituitary and two thyroid adenomas at highest dose, seven tumours were found in controls.

In rats, liver and subcutaneous tumours were induced by twice weekly gavage administration at 70 mg/kg b.w. for 22 months, and to a lesser extent following a subcutaneous implant of 15 mg/kg b.w. observed over two months. A low survival rate was a complicating factor in these studies. In a two year dietary study, 600 mg/kg diet induced an increase in thyroid C-cell carcinoma in male rats only. It is possible that a maximum tolerated dose was not achieved in the dietary study.

In a study on mice, oral administration of ziram from seven days to 78 weeks of age first by gavage (4.6 mg/kg b.w.) then at 15 mg/kg of diet from weaning age, induced no increase in tumours. Similarly no oncogenic potential was observed in mice over a six month period following daily oral administration of 75 mg/kg b.w. for 20 weeks, nor during 78 weeks of observation following a single subcutaneous injection of approximately 46 mg/kg b.w. at weaning. Furthermore, an increased incidence of alveolar/bronchiolar adenomas was observed only in female mice fed 1200 mg/kg diet. This study was complicated by an intercurrent Sendai virus infection.

Ziram can react with nitrite under mildly acid conditions to form N-nitrosodimethylamine, which is carcinogenic in several animal species.

Mutagenicity:

Ziram was mutagenically active in base-substitution sensitive *S. typhimurium* strains TA 1535, TA 100, TA 1534 and TA 1530 but not TA 1537, TA 1538, TA 98, C46, TA 1531 and TA 1532. No increase in the number of recessive lethals in *Drosophila melanogaster* (929 chromosomes) was obtained with ziram. No significant increase in gene conversion occurred in *S. cerevisiae* although metabolic activation systems were not used. An increased number of chromosome aberrations in metaphases of bone marrow cells were found in mice treated with 100 mg/kg b.w. orally. Approximately six times higher frequency of chromosome and chromatid aberrations were observed in metaphases of culture peripheral lymphocytes from workers handling ziram.

Reproduction: Some female rats receiving ziram at 50 mg/kg b.w./day for two months or more became sterile; some fetuses that were conceived were resorbed and some that were born had abnormal tails. Male fertility was not affected.

Teratogenicity: See section above.

Irritation and sensitization: Ziram was found to be a primary skin irritant with a threshold limit value of 10% concentration in a 24 hour occluded patch test in guinea pigs and, it was also shown to have mild to moderate contact hypersensitivity potency in a guinea pig maximization test.

Neurotoxicity: No information available.

Metabolism: Ziram has been shown to be an inhibitor of many enzymes. It is inhibitory to the oxidation of succinate, alpha-ketoglutarate, glutamate and isocitrate as well as on oxidative phosphorylation by isolated liver mitochondria. It also inhibits aldehyde dehydrogenase and dopamine-oxidase. It induces the accumulation of acetaldehyde in the blood stream following ethanol treatment.

- 2.1.8 Modification of toxicity - No available information.

2.2 TOXICOLOGY - MAN

2.2.1 Absorption - Ziram is poorly absorbed from the gastrointestinal tract or through the intact skin. It may be absorbed from the respiratory tract.

2.2.2 Dangerous doses - There is no information regarding doses leading to illness. The probable oral lethal dose for humans is 50 to 500 mg/kg b.w.

Repeated: No available information.

2.2.3 Observations on occupationally exposed workers - Several collective farm workers who used a 70% formulation of ziram to treat seed experienced irritation of the skin, nose, throat and eyes, gastritis, and a slight reduction in haemoglobin.

Less severe irritation of the skin and upper respiratory tract was encountered in a factory where the air concentration of ziram was 0.77-3.7 mg/m³.

Possible inhibition of cholinesterase and changes in the bioelectric activity of the muscles during voluntary motion were reported in workers. Abnormal chromosomes or chromatids were reported in 5.9% of cultured lymphocytes of workers with three to five years exposure to ziram.

2.2.4 Observations on exposure of the general population - No available information.

2.2.5 Observations on volunteers - No available information.

2.2.6 Reported mishaps - The ingestion of 0.5 l of ziram solution of unknown concentration was fatal within a few hours. Findings included focal necrosis of the mucosa of the small intestine, congestion and microscopic edema of many organs, haemorrhages, focal atelectases, acute emphysema and desquamation of alveolar and bronchial epithelium.

2.3 TOXICITY TO NON-MAMMALIAN SPECIES

2.3.1 Fish - No information available.

2.3.2 Birds - LD₅₀ Wild Bird 100 mg/kg b.w.

Ziram has been shown to have an adverse effect on body weight, to retard testicular development, and to induce degeneration in seminiferous epithelium of mature fowl.

2.3.3 Other species - No information available.

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)

All liquid formulations over 70%, category 3

All other liquid formulations, category 4

All solid formulations over 28%, category 4

All other solid formulations, category 5

3.2 TRANSPORTATION AND STORAGE -

Formulations in categories 3 and 4: Should be transported or stored in clearly labelled rigid and leakproof containers and away from containers of food and drink. Storage should be under lock and key and secure from access by unauthorized persons and children.

Formulations in category 5: Should be transported or stored in clearly labelled, leakproof containers out of reach of children away from food and drink.

3.3 HANDLING -

Formulations in categories 3 and 4: Protective clothing (see part 4) should be provided for those handling concentrates. Adequate washing facilities should be available close at hand. Eating, drinking and smoking should be prohibited during handling and before washing after handling. Adequate ventilation must be maintained.

Formulations in category 5: No special facilities other than those for handling of any chemical need be required. Adequate ventilation must be maintained.

3.4 DISPOSAL AND/OR DECONTAMINATION OF CONTAINER - If not decontaminated, container must either be burned or crushed and buried below topsoil. Care must be taken to avoid subsequent contamination of water sources. Container may be decontaminated (for method see paragraph 4.3). Decontaminated containers should not be used for food, feed or drinking water.

3.5 SELECTION, TRAINING AND MEDICAL SUPERVISION OF WORKERS -

Formulations in categories 3 and 4: Pre-employment medical examination for workers is desirable. Workers suffering from active hepatic, renal or skin disease should be excluded from contact. Training of workers in techniques to avoid contact and the need for strict abstention from alcohol use prior to and after ziram use is essential.

Formulations in categories 5: Warning of workers to minimize contact and about the dangers of alcohol use prior to and after ziram use is essential.

3.6 ADDITIONAL REGULATIONS RECOMMENDED IF DISTRIBUTED BY AIRCRAFT -

All formulations: Pilots and loaders should have special training in application methods. Flagmen if used, should wear a broad brimmed hat, a facial mask and coveralls, and be located well away from the dropping zone.

3.7 LABELLING -

Formulations in categories 3 and 4, Minimum cautionary statement:

"WARNING - POISON"

(skull and cross bones insignia)

Ziram is a dithiocarbamate; a metabolic poison of slight acute toxicity and possible long term toxic effects. It is a primary skin irritant; avoid contact with skin and eyes. Inhalation of dust or spray, or swallowing the compound may be dangerous. Wear protective gloves and clean protective clothing when handling this material. Bathe immediately after work. Ensure that containers are closed and 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. Maintain adequate ventilation during use. 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. Avoid alcohol use for at least 10 days after exposure. There is no specific antidote, treatment must be systematic.

Formulations in category 5 - Minimum cautionary statement - This formulation contains ziram, it is poisonous if swallowed. Keep the material out of reach of children and well away from food stuffs, animal feed and food containers. Maintain adequate ventilation during use. Avoid alcohol use prior to and after ziram use.

3.8 RESIDUES IN FOOD -

Maximum residue levels: Maximum residue levels have been recommended by the Joint FAO/WHO Meeting on Pesticide Residues.

4.0 PREVENTION OF POISONING IN MAN AND EMERGENCY AID

4.1 PRECAUTIONS IN USE

- 4.1.1 General - Ziram is a dithiocarbamate of slight acute toxicity and possible long term toxic effects. In addition to its inherent toxicity it induces an alcohol intolerance similar to that of Antabuse (disulfiram), a related dithiocarbamate. It is slowly absorbed by the oral and dermal routes and by inhalation of spray mist or dust. A primary irritant, avoid contact to skin and eyes, spills must be washed immediately from the skin and eyes. Adequate ventilation is essential.
- 4.1.2 Manufacture and formulation - Formulation should not be attempted without advice from the manufacture of the technical product. Although volatility is low, vapour and dusts should be controlled preferably by mechanical means. Protective equipment for the skin and respiratory protection are essential; adequate ventilation is also essential.
- 4.1.3 Mixers and applicators - When opening the container and when mixing, care should be taken to avoid contact with the mouth and eyes. Maintain adequate ventilation during handling; coveralls and gloves should be worn. Mixing if not mechanical, should always be carried out with a paddle of appropriate length. The applicator should avoid working in spray mists and avoid contact with mouth. Splashes must be washed immediately from the skin or eyes with large quantities of water. Before eating, drinking or smoking, hands and other exposed skin should be washed.
- 4.1.4 Other associated workers (including flagmen in aerial operations) -
Persons exposed to ziram and associated with its application should observe the precautions described in 4.1.3 under "Mixers and applicators".
- 4.1.5 Other populations likely to be affected - With correct application and appropriate warnings of use the general public is unlikely to be exposed to hazardous amounts of ziram. Warnings of use are essential; there are reports of contact skin irritation in sensitised persons following exposure after correct horticultural applications and after continuous use of vulcanized rubber or plastic products contaminated with ziram during their manufacture.
- 4.2 ENTRY OF PERSONS INTO TREATED AREAS - Unprotected persons should be kept out of treated areas until the spray solution is dry.
- 4.3 DECONTAMINATION OF SPILLAGE AND CONTAINERS - Residues in containers should be dissolved in a combustible solvent (alcohol, benzene, etc.) and burned in a furnace. The empty containers may be decontaminated by rinsing two or three times with a combustible solvent, the rinse burned. An additional rinse should be carried out with the 15% calcium hypochlorite solution which should remain in a container overnight, and be poured into a deep pit with abundant water. Impermeable gauntlets should be worn during this work and a soakage pit should be provided for the rinsings. Decontaminated containers should only be used for marking road works, etc. Spillage of ziram and its formulations should be removed by washing with 15% calcium hypochlorite solution and then rinsing with large quantities of water. Drain into a deep pit or sewer with abundant water.

4.4 EMERGENCY AID

- 4.4.1 Early symptoms of poisoning - Early symptoms may include dizziness, confusion, drowsiness, lethargy, ataxia, headaches, or coma; nausea, vomiting, diarrhoea and stomach pains; muscle weakness and ascending paralysis; respiratory paralysis. Skin rash and eye irritation may occur as a result of direct contact.
- 4.4.2 Treatment before person is seen by a physician, if these symptoms appear following exposure - The person should stop work immediately, remove all contaminated clothing, wash the affected skin with soap and water. Flush contaminated eyes with fresh water for 10-15 minutes. If the compound was ingested and the victim is alert, induce vomiting if it has not already occurred. Provide artificial respiration if required, preferably by mechanical means. Prevent consumption or other contact with alcohol. Contact a doctor immediately, give supportive care and remove the patient to hospital as soon as possible.

5.0 FOR MEDICAL AND LABORATORY PERSONNEL

5.1 MEDICAL DIAGNOSIS AND TREATMENT IN CASES OF POISONING

- 5.1.1 General information - Ziram is a dithiocarbamate pesticide of slight acute toxicity and possible long term toxicity. It is used as a protective fungicide on fruit and vegetable crops and in several manufacturing processes. It is absorbed from the gastrointestinal tract; by inhalation of dust or spray mist, and through the intact skin. Ziram induces alcohol intolerance, similar to that of Antabuse (disulfiram).
- 5.1.2 Symptoms and signs - Symptoms of poisoning include nausea, vomiting, abdominal pain, diarrhoea, anorexia and weight loss; headaches, lethargy, dizziness, ataxia, confusion, drowsiness and coma; suppression of tendon reflexes; initial hypotonia progressing to flaccid paralysis (Landry's syndrome); respiratory paralysis. Severe dermatitis and eye inflammation can occur after local contamination.
- 5.1.3 Laboratory - Due to rapid metabolism and excretion, detection of ziram in blood is generally not possible. Detection of ziram metabolites in urine may confirm absorption but will not necessarily reflect the degree of poisoning. Skin testing may be useful in identifying sensitization to ziram. Treatment should not be deferred pending laboratory results.
- 5.1.4 Treatment - There is no specific antidote; provide symptomatic and supportive treatment. For contact poisoning, remove all contaminated clothing and wash the affected skin and hair with soap and water; flush contaminated eyes with fresh water for 10-15 minutes. If ziram has been ingested, if the patient is alert and if vomiting has not already occurred, induce vomiting, preferably with Syrup of ipecac. Continue to observe patient for signs of depression, consciousness level and/or respiration. If these signs occur, gastric intubation, aspiration and lavage should be performed immediately. Lavage with isotonic saline or sodium bicarbonate solution should be followed by activated charcoal by intubation to limit absorption of any residual ziram in the gastrointestinal tract. If the irritant properties of ziram have not already induced a bowel movement, give a mild cathartic (e.g. magnesium sulfate). Intravenous administration of glucose and ascorbic acid (0.2 g/min up to one gram total) may be useful to accelerate the excretion of unreacted absorbed ziram. Provide artificial respiration if necessary, preferably by mechanical means. In extreme cases, if the patient is unconscious or in respiratory distress, oxygen should be provided. The patient should avoid fats, oils and lipid solvents which might enhance absorption and prohibit all forms of ethanol consumption for at least three weeks.
- 5.1.5 Prognosis - If the acute toxic effect is survived, the chances of complete recovery are very good.

5.1.6 References of previously reported cases -

Buklan, A. I. (1974), Sud-med. Ekspert, 17:51

Chernov, O. V. (1968), Gig. Tr. Prof. Zabol., 12:35-37

Martson, L. V. and Pilinskaya, M. A. (1971), Gig. Sanit., 36:107-108

5.2 SURVEILLANCE TESTS - There are no readily available techniques to determine the degree of exposure prior to the appearance of symptoms.

5.3 LABORATORY METHODS

5.3.1 Detection and assay of compound -

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Lowen, W. K. and Pease, H. L. (1964), Anal. Methods Pestic.,
Plant Growth Regul. Food Addit., 3:69

McLeod, H. A. and McCully, K. A., (1969), J. Ass. Off. Analyt. Chem., 1226-1240

Supin, G. S. et al. (1973), Khim. Sel Khoz., 11:840-842

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