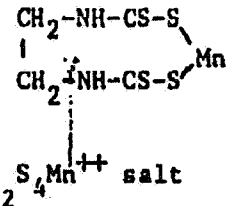
Trade Name: Crystal Maneb, Riverside Maneb 5 Dust Fungicide, Manzate, Dithane

Common Name: Maneb

Chemical Name: Manganous ethylenebisdithiocarbamate.

Structural Formula:



Empirical Formula: $C_4H_8N_2S_4Mn^{++}$ salt

Physical properties: Pure: yellow crystalline solid decomposes before melting. Tech: light-coloured solid.

Chemical properties: Stable under ordinary storage conditions but decomposes more or less rapidly when exposed to moisture or to acids. In presence of moisture decomposition proceeds with formation of polymeric ethylenethiuram monosulphide. Soluble in water slightly, insoluble in most organic solvents.

Use: fungicide on apples, apricots, cantaloupes, cabbage, carrots, celery, cucumbers, lettuce and endive, lima beans, onions, peanuts, potatoes, roses, sugar beets, tomatoes. No tolerances set on peanuts.

Company: Crystal Chemical Co., Riverside Industries.
E.I. duPont de Nemours & Co., principal manufacturers

Data obtained from E.I. du Pont de Nemours & Co., Grasselli Chemicals Dept/ and from Report No. 16-57, Haskell Laboratory for Toxicology and Industrial Medicine

Summary

Acute Rat Oral:	(1) ALD = 7500 mg/kg (2) LD_{50}=6750 (6193-7358) mg/kg ALD = 6400 mg/kg
Acute Guinea Pig Oral:	ALD = 6400 mg/kg
Subacute Rat Oral(10 days):	1500 mg/kg/day dietary level produced death in one rat after 8 days, five survived 10 days. 1275 mg/kg/day administered to six rats for ten treatments caused weight loss, discomfort, and weakness in the hind legs which progressed to paralysis in one rat. No gross pathological changes were found.
Subacute Guinea Pig Oral (10 days):	1500 mg/kg/day produced severe weight loss and gastroenteritis and was discontinued after the third treatment
Subacute Guinea Pig Dermal (2 weeks):	slight skin irritation noted. After a delay of two weeks the material was reapplied. No evidence of sensitization was noted.
Subacute Rat Feeding (3 months):	No significant effect level-0.01% level. No pathology noted in males fed 0.1%. At this level thyroid hyperplasia was noted in females.
chronic Rat Feeding Study (2 years):	No change in growth rate noted at 0.0025% level, 0.025% or males fed 0.125%. Food efficiency appeared

	lower in animals in higher dosage groups. Adenomatous thyroid hyperplasia noted in higher dosage groups also.
Chronic Dog Feeding (one year)	No significant Effect level 20mg/kg Higher dosage levels produced weakness, hypotonicity, decrease body weights, degenerative myopathies, and paralysis which was dose related.
Three Generation Rat Reproductive Study (Manzate D-88.0% Maneb)	No changes in the various parameters of reproduction and lactation were noted.

Acute Rat Oral

Raw Data not included in the material in our files

Acute Guinea Pig Oral

Raw Data not included in the material in our files.

Subacute Rat Oral (10 days)

Six rats fed 1500 mg/kg/day (1/5 LD_{50}) produced death in one animal after the eighth treatment. The other five survived the ten day treatment. Gross pathologic specimens revealed gastroenteritis only.

No raw data on this study is to be found in our files.

Subacute Rat Oral (10 days)

1275 mg/kg/day fed to six rats for ten days caused weight loss, discomfort, and weakness in the hind legs which progressed to paralysis in one rat. No pathological changes were found.

No raw data on this study is to be found in our files.

Subacute Guinea Pig Oral (10 days)

1500 mg/kg/day of the test material fed to six guinea pigs produced weight loss, diarrhea and gastroenteritis. The experiment was terminated after the third feeding because of the poor condition of the animals. Three guinea pigs survived.

No raw data on this study is to be found in our files.

Subacute Guinea Pig Dermal (two weeks)

Samples of the test material were applied to the intact skin of guinea pigs as a 20% aqueous paste, applied q.o.d. for two weeks. Two weeks after the termination of the experiment a final application was made to test skin sensitization.

Results

Results

Maneb produced only a mild irritation and showed no evidence of skin sensitizing properties.

Subacute Rat Feeding (three months)

Five each male and female rats were fed dietary levels of 0, 1%, 0.1%, 0.01% maneb for a period of ninety days.

Results

At the termination of the experiment only two rats out of the ten survived the 1% dietary level. No deaths occurred in animals fed the lower dosage levels. In these groups the rats were noted to have normal weight gains and appearance. Post mortem examination revealed thyroid hyperplasia in female rats fed 0.1% maneb. Definite evidence of thyroid hyperplasia was noted in animals of both sexes on the 1% feeding level.

An increase in the liver/body weight ratio which was marked in the two survivors at the 1.0% dietary level, moderate in males and females at the 0.1% dietary level, and in females but not males at the 0.01% dietary level was noted.

Chronic Rat Feeding Study (two years)

Twenty-five each male and female rats were fed dietary levels of 0, 0.25, 0.125, 0.025. and 0.0025% maneb for a period of two years.

Results

No signs of toxicity was noted in animals on the 0.25 and 0.0025%

dietary levels. In those fed the 0.25% dietary level it caused:

(a) A lower growth rate, slightly lower food consumption and initially lower food efficiency.

(b) No increase in mortality during the first year, but a slight increase during the second; the differences among the several groups in percent mortality and the mean age at death or sacrafice, however, were not statiatically significant.

(c) Lower plasma protein bound iodine, indicating a depression in circulating thyroid hormone.

(d) An increase in thyroid weight, and epithelial hyperplasia, nodule formation and adenoma of the thyroid.

(e) An increase in the liver/body weight ratio which was not accompanied by histological changes in the liver.

(f) Degenerative changes in the muscle of the hind legs.

Analyses indicated that maneb was not stored by body tissues.

Chronic Dog Feeding (One year)

Two dogs were fed the test material in the form of gelatin capsules (the material mixed with food at higher levels was unpalatable) at dosage levels of 0, 2, 20, 75, and 200 mg/kg/day for a period of one year.

Results

Dogs fed 2 mg/kg maneb for one year showed no signs of toxicity. One dog fed 20/mg/kg showed mild decrease in body weight, appetite, and a change in blood pressure which was not elucidated in the text.

A temporary period of weakness in the hind legs was also noted. The other dog fed the 20/mg/kg dosage level was noted to have a slight rise in plasma cholesterol.

Dogs fed 75 mg/kg/day showed loss of weight and appetite, weakness and hypotonicity of the hind legs, blood pressure changes, increase in blood cholesterol in one animal, and myopathy.

Animals fed 200 mg/kg showed all of the above signs to a greater degree and in addition, paralysis of the hind legs, anemia, polyuria, proteinuria, increase in urinary creatine, and degenerative changes in the central nervous system and muscles.

There was no noted thyroid pathology or decrease in the PBI. The neurological effects were much more pronounced in the dogs than in the rats.

Three Generation Rat Reproductive Study (Manzate D-88.0% Maneb)

The testmaterial was fed to male and female rats for three months at dosage levels of 0.0, 0.0125, and 0.025% (based on the active ingredient). At the end of the three month period a reproduction study was initiated within each group with 15 male and 16 female rats in which F_{1a} and F_{1b} litters were cast. Sixteen male and 16 female rats were selected from each of the three groups of the F_{1b} litter and continued on their respective diets for three months, at which time they were bred within groups to produce the F_{2a} and F_{2b} litters. This same procedure was followed with the F_{2b} litter to produce the F_{3a} and F_{3b} litters. Ten male and ten female weanling rats were selected from the control and test groups of the F_{3b} litter and subjected to necropsy.

Results

There were no changes which could be attributed to drug toxicity in the following reproductive and lactation parameters: Number of pregnancies, number of pups born, number of pups born alive, fertility index, gestation index, viability index, lactation index.

No gross or histopathologic findings which could be attributable to toxicity of the test material were found in the animals of the F_{3b} litter.

Maneb has a low order of acute toxicity when administered by the oral and dermal routes. No data is included in our files on acute inhalation toxicity. I do note on the label precautionary statements against oral or inhalation exposure.

The no significant effect level of Maneb in rats in two year chronic rat feeding studies is 0.025% (250 ppm).

The no significant effect level of Maneb in dogs in one year chronic feeding studies is 20 mg/kg/day (800 ppm).

Pending the receipt of acute inhalation data I do not believe that maneb produces a significant human health hazard when used according to the directions on the label.

This product has no tolerances set for peanuts. I note that one of the labels submitted for reregistration states usage for peanuts only. I trust the U.S.D.A. will deny this registration.