<u>EXTOXNET</u>

Extension Toxicology Network

A Pesticide Information Project of Cooperative Extension Offices of Cornell University, Michigan State University, Oregon State University, and University of California at Davis. Major support and funding was provided by the USDA/Extension Service/National Agricultural Pesticide Impact Assessment Program.

Pesticide

Information

Mancozeb

Profile

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TRADE OR OTHER NAMES

Some trade names include Dithane M-45, Manzate 200, Mancozeb, Fore, Green-Daisen M, Karamate, Mancofol, Zimaneb, Manzeb, Policar, Dithane- Ultra Nemispot, Nemispor, Riozeb, Mancozin, Manzin. Common names include mancozeb and manzeb.

REGULATORY STATUS

Mancozeb is registered as a general use pesticide by the U.S. Environmental Protection Agency (EPA). In July 1987, the Environmental Protection Agency announced the initiation of a special review of the ethylene bisdithiocarbamates (EBDCs), a class of chemicals to which mancozeb belongs. This Special Review was initiated because of concerns raised by laboratory tests on rats and mice. The EPA was concerned about

- a. potential effects on the general population from dietary exposure to residues left on food crops and
- b. potential occupational health risks to workers who handle and/or apply EBDC pesticides.

As part of the Special Review, EPA reviewed data from market basket surveys and concluded that actual levels of EBDC residues on produce purchased by consumers are too low to affect human health. The EPA concluded its Special Review in April, 1992 with new label requirements for protective clothing to be worn by industrial and agricultural workers, and with the establishment of a 24-hour reentry period for agricultural workers. Many homegarden uses of EBDCs have been canceled because the EPA has assumed that home users of these pesticides do not wear protective clothing during application (<u>18</u>). Toxicity data reviewed by the EPA as part of their

Special Review of EBDCs are included in this document under "Toxicological Effects."

Containers of this fungicide bear the signal word "CAUTION" (2).

INTRODUCTION

The EBDCs are fungicides used to prevent crop damage in the field and to protect harvested crops from deterioration in storage or transport (21). Mancozeb is used to protect many fruit, vegetable, nut and field crops against a wide spectrum of diseases, including potato blight, leaf spot, scab (on apples and pears) and rust (on roses). It is also used for seed treatment of cotton, potatoes, corn, safflower, sorghum, peanuts, tomatoes, flax and cereal grains (2, 16, 17). Mancozeb is not taken up from the soil by plants (6). It is a combination of two other chemicals of this class, maneb and zineb (9). Mancozeb is available as dusts, liquids, water dispersible granules, as wettable powders, and as ready-to-use (R-T-U) formulations (17).

TOXICOLOGICAL EFFECTS

ACUTE TOXICITY

Mancozeb has a very low acute toxicity to mammals. No toxicological effects were observed in a long term study with rats fed doses of 5 mg/kg (16). The major routes of exposure to mancozeb are through the skin or from inhalation (13). In spray or dust forms, the EBDCs are moderately irritating to the skin and respiratory mucous membranes. Symptoms of poisoning from this class of chemicals include itching, scratchy throat, sneezing, coughing, inflammation of the nose or throat, and bronchitis (9, 19). There is no evidence of 'neurotoxicity,' nerve tissue destruction or behavior change, from the EBDCs (9). However, dithiocarbamates are partially chemically broken down, or metabolized, to carbon disulfide, a neurotoxin capable of damaging nerve tissue (5).

The amount of a chemical that is lethal to one-half (50%) of experimental animals fed the material is referred to as its acute oral lethal dose fifty, or LD50. The oral LD50 for mancozeb ranges from 4,500 to 11,200 mg/kg in rats. When applied to the skin of rabbits, its dermal LD50 is 5,000 to 15,000 mg/kg (2, 13, 16, 17). It is a mild skin irritant and sensitizer, and a mild to moderate eye irritant in rabbits (4). Agricultural workers handling crops treated with mancozeb have developed sensitization rashes (16).

CHRONIC TOXICITY

In a two-year study dogs were fed doses of 0, 0.625, 2.5 or 25 mg/kg of mancozeb. Lower iodine uptake was observed after 24 months in dogs fed the two highest doses, while no difference was observed between those dogs fed 0 and 0.625 mg/kg (<u>16</u>).

Mancozeb is comparable to another chemical, maneb, on which the following longterm studies have been conducted. A two-year feeding study on rats indicated that 6.25 mg/kg of maneb in the diet is the no observable effect level (NOEL) for rats. However, the next and highest level that was fed to rats in this two-year study did produce signs of poisoning. A one-year feeding study in dogs concluded that 20 mg/kg/day is a NOEL for dogs. Toxic effects were seen in the dogs at daily doses of 75 mg/kg and 250 mg/kg (<u>4</u>).

The ethylene bisdithiocarbamate pesticides (EBDCs), which include mancozeb, are generally considered to have low short-term mammalian toxicity. A major toxicological concern, however, is ethylenethiourea (ETU), an industrial contaminant and a breakdown product of mancozeb and other EBDC pesticides. In addition to having the potential to cause goiter, a condition in which the thyroid gland is enlarged, this metabolite has produced birth defects and cancer in experimental animals. ETU has been classified as a probable human carcinogen by the EPA (18). ETU can be produced when EBDCs are used on stored produce, and also when fruit or vegetables with residues of these fungicides are cooked ($\underline{8}$).

Reproductive Effects

In a three-generation rat study with mancozeb at a dietary level of 50 mg/kg there was reduced fertility but no indication of embryo toxic or teratogenic effects. In another study in which pregnant rats were exposed to mancozeb by inhalation, toxic effects on the pups were observed only at doses (55 mg/m3) that were also toxic to the dams $(\underline{16})$.

Teratogenic Effects

No teratogenic effects were observed in a three-generation rat study with mancozeb at a dietary level of 50 mg/kg (<u>16</u>). Specific developmental abnormalities of the body wall, central nervous system, eye, ear and musculoskeletal system were observed in experimental rats which were given 1,320 mg/kg of mancozeb on the 11th day of pregnancy (<u>10</u>). When it was inhaled at concentrations of 0.017 milligrams per liter (mg/l), mancozeb was not teratogenic to pregnant rats (<u>4</u>). Teratogenic activity was found in mice given 1,320 mg/kg of maneb (<u>11</u>).

In pregnant rats fed 5.0 mg/kg/day, the lowest dose tested, developmental toxicity was observed in the form of delayed hardening if the bones of the skull in offspring. ETU has also been shown to be teratogenic in hamsters, but not in mice (<u>18</u>).

Mutagenic Effects

A data gap exists in the information available on the mutagenicity of mancozeb and ETU. Mancozeb was found to be mutagenic in one set of tests, while in another it did not cause mutations (13). Mancozeb is thought to be similar to maneb, which was not mutagenic in a test called the Ames Test (4).

Carcinogenic Effects

Ethylenethiourea (ETU), a metabolite of the class of chemicals in which mancozeb is included, has caused cancer in experimental animals and has been classified as a probable human carcinogen by the EPA (9, 13, 18, 21).

Organ Toxicity

Several studies of the effects of EBDCs on test animals have shown rapid reduction in the uptake of iodine and swelling of the thyroid (i.e. goiter). In one study, a marked reduction of iodine uptake was measured 24-hours after administration of a large dose of maneb, another EBDC fungicide. A 90-day study of the effects of ETU, a common metabolite of the EBDCs on rat thyroids revealed a NOEL of 5 ppm (0.25 mg/kg/day) (9, 16, 18).

Fate in Humans and Animals

The EBDC fungicides break down in mammalian tissues into ethylene thiourea, ETU, a metabolite which has caused goiter and cancer in laboratory animals (9, 18).

Research shows that mancozeb is rapidly absorbed into the body from the gastrointestinal tract, distributed to various target organs and almost completely excreted in 96 hours. ETU is the major metabolite. After a single dose, less than one ppm ETU residues were measured in the thyroid and liver. After 24 hours, these residues were not detectable (<u>13</u>). Blood detection of ethylene bisdithiocarbamate is rarely possible, although there are methods for detecting the metabolite ethylene thiourea in urine (<u>9</u>).

ECOLOGICAL EFFECTS

Effects on Birds

Mancozeb is slightly toxic to birds on an acute basis (<u>13</u>). The lethal concentration fifty (LC50) is the concentration of a material in air or water that kills half of a population that is experimentally exposed to the chemical for a given time period. The five-day LC50 for mancozeb in bobwhite quail and mallard ducklings is greater than 10,000 ppm (<u>4</u>). The EPA is currently reviewing data on the effects of mancozeb on bird reproduction (<u>18</u>).

Effects on Aquatic Organisms

Mancozeb is generally toxic to fish. It is highly poisonous to warmwater fish and at least moderately toxic to coldwater fish. Many end-use product labels warn of its toxicity to fish (13). The EPA is currently reviewing data on the potential toxic effects of mancozeb on aquatic organisms (18).

Effects on Other Animals (Nontarget species)

Mancozeb is harmful to wildlife but not hazardous to honey bees ($\underline{6}$). The 72-hour LC50 for mancozeb in crayfish is greater than 40 ppm; the 48-hour LC50 is 3.5 ppm in tadpoles ($\underline{4}$).

ENVIRONMENTAL FATE

The EBDCs are generally unstable in the presence of moisture, oxygen, and in biological systems (22). They rapidly degrade to ETU. This rapid degradation lowers the need for concern about the environmental fate of EBDCs and focuses such concern on ETU. The EPA has either called for or is currently reviewing data on the behavior of ETU in the environment (9, 14, 18).

Breakdown of Chemical in Soil and Groundwater

Because mancozeb is practically insoluble in water it is unlikely to infiltrate groundwater (17, 20). Studies do indicate that ETU, a metabolite of mancozeb, has the potential to move through the soil as a result of groundwater movement, in a process called leaching (13). ETU has been detected at 16 ppb in only one out of 1,295 drinking water wells tested (18).

The breakdown of mancozeb in soil is assumed to be comparable to that of maneb, which has a half-life of four to eight weeks under normal field conditions ($\frac{4}{2}$).

Breakdown of Chemical in Water

Mancozeb degrades in water with a half-life of one to two days at pH 5, 7 and 9 (<u>13</u>). It should be kept out of lakes, streams and ponds and should not be applied where runoff is likely to occur (<u>4</u>). This fungicide should not be stored or thrown away near or in water, since storage or disposal of mancozeb in or near bodies of water can cause contamination (<u>2</u>).

Breakdown of Chemical in Vegetation

When used as directed, mancozeb is not poisonous to plants ($\underline{6}$). A 24-hour reentry interval is required in mancozeb-treated crops because: (1) the fungicide is registered on crops which may present a great deal of residue exposure and ($\underline{2}$) the mancozeb metabolite, ETU, has been shown to produce tumors, birth defects, cell mutations and thyroid effects (13). The EBDCs can be broken down during the cooking process as well as by natural environmental processes (14).

PHYSICAL PROPERTIES AND GUIDELINES

Keep mancozeb out of reach of children, unprotected persons, livestock, and pets (4, 13). Breathing of dust or spray mist from mancozeb should be avoided. Contact with skin, eyes and clothing should also be avoided. Protective clothing including long pants, long sleeve shirt, gloves, hat and boots should be worn during mixing, loading, application and early reentry into treated fields (13, 18). Do not feed treated crop foliage to livestock (12). Water, food or feed can be contaminated by storage or disposal of mancozeb near these commodities. Empty containers should not be reused. They should be buried away from water supplies (2).

Mancozeb is a grayish-yellow powder with a musty odor (<u>19</u>) which is practically insoluble in water as well as most organic solvents. It is a polymer of maneb combined with zinc. While it is relatively stable and noncorrosive under normal, dry storage conditions, it is decomposed at high temperatures by moisture and by acid. Mancozeb may produce flammable products upon decomposition (<u>4</u>, <u>16</u>). It is also unstable in acidic conditions (<u>7</u>). It should be stored in its original sealed containers in well-aired, dry storehouses or in shaded, aired places. The temperature of the material should not go above 25 to 30 degrees C. Mancozeb containers must be stacked so that air can move freely at the bottom and sides of piles. As long as the product is stored in its unopened and undamaged original containers in well-ventilated places, its biological activity will remain stable for 2 years (<u>2</u>).

Mancozeb is stable under most conditions. It may burn, but does not readily ignite, and containers may explode in the heat of a fire. Thermal decomposition products

may include toxic oxides of carbon, nitrogen and sulfur. Suspensions of mancozeb dust in the air can ignite or explode $(\underline{19})$.

Occupational Exposure Limits:

OSHA: 5 mg/m3 ceiling (19) ACGIH: 5 mg/m3 TWA (19) NIOSH: 1 mg/m3 recommended TWA (19); 3 mg/m3 recommended STEL (19) TLV: 5 mg (Mn)/m3 (1)

Physical Properties:

CAS #:	8018-01-7
H20 solubility:	dispersible, but practically insoluble in water (7, 8, 19)
Solubility in other solvents	: practically insoluble in most organic solvents (8)
Melting point:	Decomposes without melting (7)
Vapor pressure:	Less than 10 to the minus 5 power mbar at 20 degrees C
Chemical Class/Use:	Carbamate fungicide; Ethylene bisdithiocarbamate (EBDC)

BASIC MANUFACTURER(S)

Du Pont Agricultural Products Walker's Mill, Barley Mill Plaza PO Box 80038 Wilmington, DE, 19880-0038

Review by Basic Manufacturer:

Comments solicited: October, 1992 Comments received: November, 1992

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