chemicalWATCH Factsheet

CAPTAN

Used on everything from food to shower curtains, the fungicide captan has a long and worrisome regulatory history. Classified by the Environmental Protection Agency (EPA) as a B2 or probable human carcinogen, captan is an extremely potent carcinogen, causing malignant tumors even at the lowest doses tested, and striking numerous organs including the digestive track, thyroid, adrenal gland and kidney. Captan is a mutagen, and causes fetal death, birth defects and other reproductive problems in many test animals. As early as 1969, serious concern over captan's ability to cause birth defects led the Department of Health, Education and Welfare to suggest that captan be restricted to prevent human exposure.[1] But, despite a nine year journey through EPA's Special Review process, the chemical is still widely used.

Captan is a broad spectrum, systemic fungicide, sold under many trade names including Orthocide™ and Merpan™. EPA estimates that 4-7 million pounds were used in 1990;[2] 270,000 pounds were reported used in California alone.[3] Introduced by Chevron Chemical in 1949, and registered in 1951, it is now also produced by Stauffer Chemical. Captan is a chlorinated organosulfur pesticide in the phthalimide family. It is structurally related to two other fungicides, captafol (cancelled in 1987) and folpet, as well as to thalidomide. Now banned, thalidomide is an anti-nausea drug which causes severe birth defects.

Although not generally considered acutely toxic, with a rat LD_{50} of 12,600 mg/kg, captan is very acutely toxic to animals maintained from birth on a protein deficient diet, LD_{50} = 100 mg/kg.[4] Captan is a severe eye irritant, a skin irritant and a skin sensitizer.[5]

A surprising number of studies have been done documenting captan's ability to cause cancer in animals. A 1977 National Cancer Institute (NCI) study on mice found rare adenocarcinomas of the duodenum (the portion of the small intestine closest to the stomach) in both male and female mice, with significant increases in males.[6,7]

In 1981, Chevron did its own lifetime study of mice using high doses of captan. There was a significant and dose-related increase in adenocarcinomas and adenomas of the duodenum, in both genders.[8] In 1983, Chevron, not yet convinced, had another mouse study done using much lower doses of captan with emphasis on the gastrointestinal tract.[9] Even at the lowest dose, 100 ppm, both genders developed not only adenomas and adenocarcinomas of the duodenum, but also of the stomach and other parts of the small intestine, thus providing further evidence of the carcinogenicity of captan in mice.

Captan carcinogenicity is not limited to mice. In the NCI captan study, female rats had adenomas and carcinomas of the adrenal gland and adenomas of the thyroid.[7] Stauffer and Chevron then performed yet another study on rats. Male rats developed significant dose-related adenomas and adenocarcinomas of the kidney.[10]

This evidence, along with the carcinogenicity of folpet and captafol in animals, convinced EPA that captan is indeed carcinogenic. Like captan, folpet produces intestinal tumors in mice,[11,12] while captafol induces liver, lymph and bone marrow cancers.[13]

Captan is mutagenic, producing gene mutations in microbial systems and in laboratory cultures of mammalian cells.[6] The chemical produced chromosome aberrations in cultured human embryo lung cells, kangaroo rat cells, and in Chinese hamster ovary cells.[6] Captan also interferes with DNA repair mechanisms in bacteria and cultured animal cells.[6] Dominant lethal effects were reported in a rodent study.[6]

A number of different studies have documented captan's ability to cause birth defects, fetal death, reduced litter size and reduced offspring survival in hamsters, mice, rats, chickens, dogs, and possibly monkeys. These results are particularly important in light of captan's structural similarity to the known human teratogen thalidomide.

In a 1970 study on hamsters, captan caused birth defects, including exencephaly (brain development outside a defective skull) and fused ribs.[14] A dose-response trend was evident. Another study on hamsters noted fetotoxicity, with fewer live fetuses, increased fetal resorption, and rib anomalies.[15]

An earlier 1968 NCI study reported increased fetal mortality, reduced fetuses per litter and reduced fetal weights in two strains of mice, as well as an increased number of abnormal fetuses, largely resulting from microphthalmia (small eyes) in one strain.[16]

In an unusual study, captan was administered to pregnant dogs throughout gestation.[17] There was an increase in the number of pups and litters with birth defects, the number of litters with stillbirths and the percentage of pups stillborn. The defects included crooked tails, gastroschisis (fis-

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Pesticides and You

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sure of the abdominal wall, usually with protrusion of the intestines), single kidney and hydrocephalus. None of the abnormalities were present in control dogs.

EPA notes that, "A monkey study was reported as negative (however, three abortions among seven monkeys at the highest dosage could be a matter of concern)."[6] And a chick embryo study indicates that captan and a metabolite cause birth defects in birds.[18]

A reproduction study in rats found a significant, dose-related increase in fetal mortality, with only 17 percent of fetuses surviving to birth in the high dose group, versus 66 percent in the control rats.[19] Studies in rats and rabbits found reduced pup litter weights.[20,21]

In a series of studies on mice and rats, captan administered up to several weeks before mating, to males only, caused statistically significant increases in the number of fetal deaths in both mice and rats.[22] Furthermore, in a two-generation mouse study, in which males were treated before the first mating, there were fewer live pups born in the first generation and decreased offspring survival in both the first and second generation offspring.[23]

Nonetheless, EPA holds that captan is not a teratogen, and acknowledges only reduced pup litter weights as a reproductive effect of concern.[24]

The metabolism of captan has been studied mostly in rats. Captan is broken down to tetrahydrophthalimide (THPI) and a derivative of the trichloromethylthio side chain which are broken down to 3-hydroxy THPI, THPAM and thiophosgene.[6] THPI is present in both plants and animals as a captan metabolite and may be of toxicological concern. Most of the metabolites are excreted through the urine, although some are also present in the feces and in expired air. In the only mouse study, radioactively-labeled captan and/or metabolites were distributed throughout the body tissues, including the testes.[25] This finding may be of particular importance given the evidence of mutagenicity and reproductive effects.

According to EPA, "The half-life of captan in soil can range from one day to more than two months, depending on soil type and moisture. Under field conditions, two to three weeks is the expected half-life."[6] In water, half-lives range from 12 hours under acidic conditions to 10 minutes under alkaline conditions.[6] The pesticide is active on leaves for about two weeks. EPA claims that captan does not demonstrate the potential to bioaccumulate or to leach.

Captan is considered very highly toxic to fish, with LC_{50}'s of 49-141 ppb. Despite this, EPA feels that because there are no uses of captan in which it is intentionally applied to water, and because it degrades rapidly in water, any damage would be only localized. Captan is not acutely toxic to birds, with pheasant and mallard LC_{50}'s greater than 5,000 ppm. It is also not acutely toxic to many beneficial mites or bees.

Captan was placed in EPA's Special Review process in 1980 because of carcinogenicity concerns, although the Agency also noted potential concerns regarding teratogenicity, reproductive effects and toxicity to aquatic organisms.[26] In 1985, the Agency announced that it intended to cancel food uses by 1987 - unless new data showed exposure to be lower than estimated.[27] At that time, EPA estimated cancer risk from dietary exposure to be between one case per thousand people and one case per ten thousand.[6] Unbelievably, a third of the dietary risk comes from milk consumption—even though there is no tolerance for captan residues in milk.[28] In the 1989 final decision, EPA cancelled 45 food uses, and suspended 13, with 11 remaining. As of August, 1992, EPA has revoked the tolerances for only ten of the 45 cancelled uses.[29] EPA's revised dietary risk estimate was one in a hundred thousand to one in a million.[24] EPA considers one additional cancer per million people to be acceptable for each carcinogenic pesticide.

In a 1992 EPA effort comparing allowable captan residues with the level of intake that EPA considers will not cause unreasonable adverse effects in humans, the Agency found that captan exposure to non-nursing infants may be as high as 5.5 times the acceptable level, while children ages one to six may be exposed to four times the allowable level.[30] Captan is regularly found in the Food and Drug Administration's multi-residue food monitoring.[31]

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