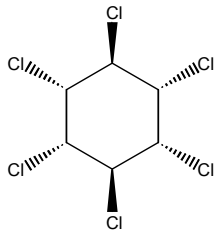
LINDANE AND OTHER HEXACHLOROCYCLOHEXANE ISOMERS
CAS No. 58-89-9
First Listed in the *Second Annual Report on Carcinogens*



CARCINOGENICITY

Lindane and other hexachlorocyclohexane isomers are *reasonably anticipated to be human carcinogens* based on sufficient evidence of carcinogenicity in experimental animals (IARC 1979, 1982, 1987, NCI 1977). When administered in the diet, technical-grade, α-, and β-hexachlorocyclohexane and lindane induced liver tumors in mice; the technical-grade material also produced lymphoreticular neoplasms in mice. When administered in the diet in two studies, the α-isomer increased the incidence of liver tumors in rats, and in one study in rats, a few thyroid tumors were observed with the γ-isomer; other studies in rats were considered inadequate. Studies in hamsters and dogs were also judged inadequate. Technical-grade hexachlorocyclohexane and the γ-isomer were inadequately tested by skin application in mice. α-Hexachlorocyclohexane increased the incidence of liver neoplasms induced in rats by *N*-nitrosodiethylamine.

There is inadequate evidence for the carcinogenicity of lindane and other hexachlorocyclohexane isomers in humans (IARC 1987). Four cases of leukemia were reported in men exposed to γ-hexachlorocyclohexane (lindane) with or without other chemicals. Cases of aplastic anemia have also been associated with exposure to this compound. Mean tissue levels of hexachlorocyclohexanes were reported to be elevated in two of three studies of autopsy patients; in one of these studies, the levels of the γ-hexachlorocyclohexane were not appreciably higher in four cancer patients than in three controls. Exposure to γ-hexachlorocyclohexane was recorded in case-control studies of soft-tissue sarcomas and of lymphomas, but it was considered insufficiently frequent for any conclusion to be drawn. An increase in lung cancer mortality was observed in agricultural workers who had used hexachlorocyclohexane (unspecified) and a variety of other pesticides and herbicides.

PROPERTIES

Lindane, the γ-isomer of hexachlorocyclohexane, is a white or colorless, crystalline solid that is soluble in water. Commercial lindane is 99% γ-hexachlorocyclohexane. Technical-grade hexachlorocyclohexane is a mixture of isomers containing 64% α-, 10% β-, 13% γ-, 9% δ-, and 1% ε-hexachlorocyclohexanes. When heated to decomposition, these isomers emit toxic fumes of hydrochloric acid and other chlorinated compounds as well as phosgene gas. Lindane is slightly soluble in mineral oils and sparingly soluble in petroleum and hydrocarbons. At 25°C, 7 ppm lindane is soluble in water. At 20°C, solubilities in the various solvents are as follows: 43.5 g lindane/100 g acetone, 28.9 g lindane/100 g benzene, 24.0 g lindane/100 g chloroform, 20.8 g lindane/100 g ether, and 6.4 g lindane/100 g ethanol (HSDB 2001).

USE

Lindane is used primarily as an insecticidal treatment for hardwood logs and lumber, seed grains, and livestock. Other major uses are as an insecticide for several dozen fruit and vegetable crops, and for personal hygiene as a scabicide and pediculicide in the form of a lotion, cream, or shampoo. Agricultural uses accounted for approximately 95% of the lindane and other hexachlorocyclohexane isomers used in 1974; the remaining uses were industrial (IARC 1974, 1979). Lindane is also used in baits and seed treatments for rodent control and has been of value in control of malaria and other vector-borne diseases (NTP 2001).

PRODUCTION

Lindane is not produced commercially in the United States (SRI 1986). The Chem sources identified one bulk supplier, two suppliers of analytical grade, and one distributor that supplied both bulk quantity and analytical grade lindane among the eleven that were listed in 1990 (Chem Sources 1991). Chem Sources (2001) identified 18 suppliers of lindane. No import or export data are available for other isomers of hexachlorocyclohexane. Benzene hexachloride (BHC), listed by HSDB as a synonym for Lindane, is no longer produced or sold for domestic use in the U.S. (HSDB 2001). Commercial production of lindane began in the United States in 1945 and peaked in the 1950s, when 15 million lb of the compound were manufactured (IARC 1974).

EXPOSURE

The primary routes of potential human exposure to lindane and other hexachlorocyclohexane isomers are ingestion, inhalation, and dermal contact. The National Occupational Exposure Survey indicated that 8,779 total workers, including 2,797 women, potentially were exposed to lindane (NIOSH 1984). Exposures were not reported for other hexachlorocyclohexane isomers. Prior to EPA regulation of lindane and other hexachlorocyclohexane isomers in 1977, approximately 480,000 workers were possibly exposed to these substances in the workplace. Pesticide applicators were at the highest risk of exposure. The possible risk of exposure for the general public is through consumption of foodstuffs contaminated with pesticide residues. Major potential dietary sources of lindane include milk, eggs, dairy products, and to a lesser extent, seafood (HSBD 2001). The dietary intake of lindane and its isomers by the U.S. population is estimated to be in trace quantities, and is undergoing a significant, steady decline. EPA's Toxic Chemical Release Inventory (TRI) listed eight industrial facilities that produced, processed, or otherwise used lindane in 1996 (TRI96 1998). The facilities reported releases of lindane to the environment, which were estimated to total 765 lb: 510 lb total air releases, 5 lb total water releases, and 250 lb total land releases. In 1999, total air and surface water discharges were 30 and 6 lb, respectively (TRI99 2001). Additional exposure information may be found in the ATSDR Toxicological Profile for Hexachlorocyclohexanes (ATSDR 1999).

REGULATIONS

EPA regulates lindane and its isomers under the Clean Water Act (CWA), Comprehensive Environmental Response, Compensation, and Liability Act (CERCLA), Federal Insecticide, Fungicide and Rodenticide Act (FIFRA), Resource Conservation and Recovery Act (RCRA), Safe Drinking Water Act (SDWA), and Superfund Amendments and Reauthorization Act (SARA). Lindane is registered under FIFRA for use as a seed and seedling treatment and is no longer used as an insecticide on wood or on fruit and vegetable crops or on livestock. EPA has proposed and established effluent guidelines for lindane from several point sources. Under CWA, EPA established a reportable quantity (RQ) of 1 lb for γ-hexachlorocyclohexane (lindane) and withdrew proposed RQs of 10 lb for other isomers of hexachlorocyclohexane. EPA has established a final RQ of 1 lb for lindane under CERCLA. Following the initiation of a Rebuttable Presumption Against Registration (RPAR), the use of pesticides containing hexachlorocyclohexane isomers other than lindane was voluntarily cancelled. Hexachlorocyclohexane is regulated as a hazardous constituent of waste under RCRA, and SARA subjects it to reporting requirements. A maximum contaminant level (MCL) and a maximum contaminant level goal (MCLG) of 0.0002 mg/L was proposed for lindane in drinking water under SDWA.

FDA regulates the presence of lindane in drinking water and drugs and prohibits its residues in animal feed.

ACGIH recommends a threshold limit value (TLV) at 0.5 mg/m^3; the potential for exposure through skin absorption was noted. NIOSH has established a recommended exposure level (REL) for lindane of 0.5 mg/m^3 as a 10-hr time-weighted average (TWA), with a skin notation. OSHA adopted a permissible exposure limit (PEL) for lindane of 0.5 mg/m^3 as an 8-hr TWA. OSHA regulates lindane and other hexachlorocyclohexanes isomers under the Hazard Communication Standard and as chemical hazards in laboratories. Regulations are summarized in Volume II, Table 102.

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