Lindane (CAS No. 58-89-9) and Other Hexachlorocyclohexane Isomers

Reasonably anticipated to be a human carcinogen First Listed in the Second Annual Report on Carcinogens (1981)



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 lindane; other studies in rats were considered inadequate. Studies in hamsters and dogs were also judged inadequate. Technical-grade hexachlorocyclohexane and lindane 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 yhexachlorocyclohexane (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 lindane were not appreciably higher in four cancer patients than in three controls. Exposure to lindane 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% E-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 (HSDB 2001).

Production

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). Lindane is no longer produced commercially in the United States (SRI 1986). 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 United States (HSDB 2001).

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 DOT

Lindane is considered a marine pollutant and special requirements have been set for marking, labeling, and transporting this material

EPA Clean Air Act

- NESHAP: Lindane (all isomers) listed as a Hazardous Air Pollutant (HAP)
- Clean Water Act
- Effluent Guidelines: Listed as a Toxic Pollutant (hexachlorocyclohexane) Water Quality Criteria: Based on fish/shellfish and water consumption = 0.019 µg/L (lindane); 0.0026 µg/L (alpha isomer); 0.0091 µg/L (beta isomer); based on fish/shellfish consumption only = 0.063 μ g/L (lindane); 0.0049 μ g/L (alpha iso-
- mer); 0.017 µg/L (beta isomer) Comprehensive Environmental Response, Compensation, and Liability Act
- Reportable Quantity (RQ) = 1 lb (lindane), 10 lb (alpha isomer)
- Emergency Planning and Community Right-To-Know Act
- Toxics Release Inventory: Listed substances subject to reporting requirements (lindane and alpha isomer)
- Reportable Quantity (RQ) = 1 lb (lindane)
- Threshold Planning Quantity (TPQ) = 1,000 lb (lindane solid in powder form particle size <100 microns, or solution or molten form); 10,000 lb (lindane - all other forms)

Resource Conservation and Recovery Act

- Characteristic Toxic Hazardous Waste: TCLP Threshold = 0.4 mg/L (lindane) Listed Hazardous Waste: Waste codes in which listing is based wholly or partly on substance - U129, F024
- Lindane listed as a Hazardous Constituent of Waste

Safe Drinking Water Act

Maximum Contaminant Level (MCL) = 0.0002 mg/L (lindane)

FDA

Maximum permissible level in bottled water = 0.0002 mg/L (lindane) Action levels for lindane in food and in animal feed range from 0.1-0.5 ppmLindane is a prescription drug subject to labeling and other requirements

OSHA

Permissible Exposure Limit (PEL) = 0.5 mg/m³ (lindane)

Guidelines

ACGIH

Threshold Limit Value - Time-Weighted Average Limit (TLV-TWA) = 0.5 mg/m³ (lindane)

NIOSH

Recommended Exposure Limit (REL) = 0.5 mg/m³ (lindane)

Immediately Dangerous to Life and Health (IDLH) = 50 mg/m³ (lindane)

REFERENCES

- ATSDR. 1999. Toxicological Profile for Alpha-, Beta-, Gamma-, and Delta-Hexachlorocyclohexanes. Update. (Final Report). NTIS Accession No. PB99-166662. Atlanta, GA: Agency for Toxic Substances and Disease Registry. 313 pp.
- ChemSources. 2001. Chemical Sources International, Inc. http://www.chemsources.com.
- HSDB. 2001. Hazardous Substances Data Base. National Library of Medicine. http://toxnet.nlm.nih.gov/ cgi-bin/sis/htmlgen?HSDB.
- IARC. 1974. Some Organochlorine Pesticides. IARC Monographs on the Evaluation of Carcinogenic Risk of Chemicals to Humans, vol. 5. Lyon, France: International Agency for Research on Cancer. 241 pp.
- IARC. 1979. Some Halogenated Hydrocarbons. IARC Monographs on the Evaluation of Carcinogenic Risk of Chemicals to Humans, vol. 20. Lyon, France: International Agency for Research on Cancer. 609 pp.
- IARC. 1982. Chemicals, Industrial Processes and Industries Associated with Cancer in Humans. IARC Monographs on the Evaluation of Carcinogenic Risk of Chemicals to Humans, Supplement 4. Lyon, France: International Agency for Research on Cancer. 292 pp.
- IARC. 1987. Overall Evaluations of Carcinogenicity. IARC Monographs on the Evaluation of Carcinogenic Risk of Chemicals to Humans, Supplement 7. Lyon, France: International Agency for Research on Cancer. 440 pp.
- NCI. 1977. Bioassay of Lindane for Possible Carcinogenicity (CAS No. 58-89-9). Natl Toxicol Program Tech Rep Ser 14: 1-99.
- NIOSH. 1984. National Occupational Exposure Survey (1981-83). Cincinnati, OH: U. S. Department of Health and Human Services. http://www.cdc.gov/noes/noes/noes3/empl0003.html.
- SRI. 1986. Directory of Chemical Producers, United States, 1985. Stanford Research Institute, Menlo Park, CA: SRI International.
- TRI96. 1998. Toxic Chemical Release Inventory 1996. Data contained in the Toxic Chemical Release Inventory (TRI). National Library of Medicine.
- TRI99. 2001. Toxic Chemical Release Inventory 1999. Data contained in the Toxic Chemical Release Inventory (TRI). National Library of Medicine. http://www.epa.gov/triexplorer/.