Sources of Exposure

General Populations

- Exposure of the general population to hexachlorocyclohexanes has declined steadily since its use as a pesticide was discontinued in 2006.
- The general population can be exposed to hexachlorocyclohexanes from ingestion of contaminated food and water; inhalation of contaminated air; or through incidental ingestion of, or dermal contact with, contaminated soils. People may be exposed through contact with old containers of lindane pesticides stored at homes or businesses. In addition, persons who use the prescription formulation of γ-HCH for scabies or lice treatment will be exposed by dermal contact.
- The hexachlorocyclohexanes in this guide are no longer commonly detected in food items.
- Small amounts of hexachlorocyclohexanes have been detected in aquatic organisms.

Occupational Populations

- Occupational exposure to hexachlorocyclohexanes may occur through inhalation or dermal contact in facilities that use, reformulate, or package these chemicals.

Toxicokinetics and Normal Human Levels

Toxicokinetics

- Hexachlorocyclohexanes are well absorbed following oral exposure. Absorption after inhalation and dermal exposure is inferred from measurements in serum in exposed humans.
- Hexachlorocyclohexanes are primarily distributed to adipose tissue, but also to the brain, kidney, muscle, blood, and other tissues. β-HCH accumulates to a greater degree than other isomers.
- Metabolism of hexachlorocyclohexanes occurs mainly via hepatic cytochrome P-450, and the primary urinary metabolites are chlorophenols. Metabolites of hexachlorocyclohexanes are excreted in the urine as conjugates of mercapturic acid, glucuronide, and sulfate.
- Hexachlorocyclohexanes are primarily excreted in the urine after oral, dermal, or inhalation exposure. Hexachlorocyclohexane isomers are also excreted in breast milk. The most persistent isomer is β-HCH: the half-life for β-HCH in blood of workers was estimated to be more than 7 years.

Normal Human Levels

- NHANES 2013–2014 reported geometric mean lipid-normalized serum concentrations as high as 242 ng/g for β-HCH. A geometric mean concentration for γ-HCH could not be calculated because the proportion of results below the lowest detectable level was too high to provide a valid result. Serum monitoring was not conducted in subsequent NHANES study periods.

Biomarkers/Environmental Levels

Biomarkers

- Hexachlorocyclohexane isomers can be measured in blood, urine, hair, adipose tissue, and semen. Of the isomers, β-HCH persists longest in the body and is often used as a marker for exposure to hexachlorocyclohexane.
- Chlorophenol metabolites of hexachlorocyclohexane can be detected in urine, but the relationship to exposure is uncertain because other chemicals are also metabolized to chlorophenols.

Environmental Levels

Air

- Monitoring data show α- and β-HCH concentrations up to 0.017 and 0.064 ng/m^3, respectively, in outdoor air in the United States.

Water

- Monitoring data collected after 2007 show α- and β-HCH concentrations up to 1.7 and 1.2 ng/L for surface water and no detections in groundwater except near former pesticide facilities or waste storage areas.

Sediment and Soil

- U.S. soil and sediment samples collected between 2007 and 2020 showed concentrations up to 0.39 µg/kg for β-HCH, while neither α- nor δ-HCH was detected. Recent monitoring data for γ- and technical-grade HCH in soil and sediment were not located.

Reference

Agency for Toxic Substances and Disease Registry (ATSDR). 2024. Toxicological Profile for Hexachlorocyclohexanes. Atlanta, GA: U.S. Department of Health and Human Services, Public Health Services.

ToxGuide™ for Hexachloro-cyclohexanes

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www.atsdr.cdc.gov

ATSDR
AGENCY FOR TOXIC SUBSTANCES AND DISEASE REGISTRY

Chemical and Physical Information

Hexachlorocyclohexanes

- Hexachlorocyclohexanes are a group of chemicals in which the six hydrogens on cyclohexane have been replaced with chlorines. There are eight hexachlorocyclohexane stereoisomers.
- Four hexachlorocyclohexanes were evaluated for this guide. They include: α-, β-, γ-, and δ-hexachlorocyclohexane (abbreviated α-HCH, β-HCH, γ-HCH, and δ-HCH).
- The hexachlorocyclohexane isomers evaluated in this guide are all solid at room temperature.
- Hexachlorocyclohexanes have musty or phosgene-like smells.
- Agricultural uses of γ-HCH were discontinued in 2006. γ-HCH is available and regulated by the U.S. Food and Drug Administration (FDA) for the pharmaceutical treatment of scabies and head lice.
- The remaining isomers of hexachlorocyclohexanes (α-, β-, and δ-HCH) occurred as byproducts during the manufacture of technical-grade hexachlorocyclohexane.

Routes of Exposure

- Inhalation – Likely route of exposure for the general and occupational populations.
- Oral – Likely route of exposure for the general population through ingestion of contaminated food, soil, or water.
- Dermal – Likely route of exposure for occupational population and for general population using medications containing hexachlorocyclohexane.

Hexachlorocyclohexanes in the Environment

- Historically, hexachlorocyclohexane has been released to the environment during its formulation process and through its use. γ-HCH can be released to wastewater via "down-the-drain" releases from consumer wash-off of treatments for lice and scabies.
- In surface waters, hexachlorocyclohexane has a slight tendency to dissolve and remain in the water column based on the water solubilities and octanol-water partition coefficients of the isomers.
- Hexachlorocyclohexane isomers are relatively persistent in the atmosphere and are capable of long-range transport.
- The hexachlorocyclohexanes in this guide are considered to possess low to moderate bioaccumulation potential.
- Hexachlorocyclohexane present in soil can leach to groundwater, sorb to soil particulates, or volatilize to the atmosphere.

Relevance to Public Health (Health Effects)

Health effects are determined by the dose (how much), the duration (how long), and the route of exposure.

Minimal Risk Levels (MRLs)

Inhalation

- No acute-, intermediate-, or chronic-duration inhalation MRLs were derived for hexachlorocyclohexanes.

Oral

- Acute-duration (≤14 days) oral MRLs of 0.08 mg/kg/day (β-HCH) and 0.003 mg/kg/day (γ-HCH) were derived.
- Intermediate-duration (15–364 days) oral MRLs of 0.002 mg/kg/day (α-HCH), 0.0006 mg/kg/day (β-HCH), and 0.0000008 mg/kg/day (γ-HCH) were derived.
- A chronic-duration (≥365 days) oral MRL of 0.0009 mg/kg/day was derived for α-HCH.

Health Effects

- Neurological effects such as tremors and convulsions have been seen in humans after higher level oral and dermal γ-HCH exposure. Seizures and convulsions, ataxia, and central nervous system depression were seen in animals exposed to higher levels of γ-HCH by oral, inhalation, and dermal routes. Ataxia and hypoactivity were also seen in rats exposed orally to higher levels of β-HCH.
- Oral exposure to α-, β-, and γ-HCH in rats or mice led to increased liver weight, hepatocellular hypertrophy, fatty degeneration, and necrosis.
- Increased perinatal mortality and increased pup liver weights (β-HCH) or decreased pup weights (γ-HCH) occurred in rats after gestational and/or lactational exposure. Developmental neurotoxicity, cardiac effects, and reproductive effects were also seen in pups exposed *in utero* to γ-HCH.
- Immune system effects were seen in animals after oral exposure to β- and γ-HCH.
- Association of hexachlorocyclohexanes to cancer in humans is complicated by the presence of other chemicals during exposure. Rats and mice exposed to α-, β-, and γ-HCH in their diets had increased incidences of liver and lung cancers.
- Hexachlorocyclohexanes have been classified by the U.S. Department of Health and Human Services as reasonably anticipated to be human carcinogens. The U.S. Environmental Protection Agency classified α-HCH as probably carcinogenic and β-HCH as possibly carcinogenic to humans. The International Agency for Research on Cancer classified γ-HCH as carcinogenic to humans.

Children's Health

- It is not known if children are more sensitive to hexachlorocyclohexane effects than adults, but β- and γ-HCH are developmental toxicants in animals, and young animals are more susceptible to the neurotoxic effects of γ-HCH than older animals.