Sources of Exposure

General Populations

- The general public is most likely exposed to chloroform through ingesting food and water containing chloroform, inhaling contaminated air, and dermal contact with chloroform-containing water.
- The primary route of exposure is from the small amount of chloroform produced in drinking water as a byproduct of chlorination.
- General population exposures are expected to be low when not near a chloroform source.

Occupational Populations

- Occupational exposure to chloroform may occur via inhalation of contaminated workplace air or direct dermal contact with vapor or liquid.
- Workers involved in manufacture or who use chloroform and operators at incinerators, wastewater facilities, paper, or pulp plants may be exposed to chloroform.
- Workers with increased exposure to chlorinated water, such as professional cleaning staff or lifeguards at chlorinated indoor and outdoor pools, may be exposed to chloroform.

Toxicokinetics and Normal Human Levels

Toxicokinetics

- Absorption of chloroform can occur through the lungs, gastrointestinal tract, and skin.
- Absorbed chloroform is distributed throughout the body. Based on blood-tissue partition coefficients, the equilibrium distribution would be in the following order: fat>>liver>kidney≥ other tissues.
- Chloroform is metabolized by mixed function oxidases (CYP2E1) in the liver, kidney, and other tissues to form reactive intermediates such as phosgene.
- Absorbed chloroform is excreted primarily through the lungs as chloroform. Metabolites are excreted primarily through the lungs as carbon dioxide and in urine to a lesser extent.

Normal Human Levels

- The geometric mean concentration of chloroform in blood was 6.32 pg/mL in NHANES 2011–2012.

Biomarkers/Environmental Levels

Biomarkers

- Chloroform levels can be measured in blood, tissue, urine, breast milk, and expired air, with blood and expired air being the most validated.
- Presence of chloroform or its metabolites in biological fluids and tissues may also reflect exposure to other chlorinated hydrocarbons (e.g., carbon tetrachloride)

Environmental Levels

- Air:
  - The average ambient air concentration across 125 U.S. locations in 2022 was 0.032 ppbv.
- Water:
  - The average groundwater concentration from 343 U.S. samples in 2022 was 1.6 ppb.
  - The average surface concentration from 10 U.S. samples in 2022 was 0.23 ppb.
  - Most drinking water samples tested in the United States between 1991 and 2010 were <0.2 ppb.
- Soil:
  - No recent monitoring data for ambient soil levels in the United States are available.

Reference

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

ToxGuide™ for Chloroform

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U.S. Department of Health and Human Services
Public Health Service
Agency for Toxic Substances and Disease Registry
www.atsdr.cdc.gov

ATSDR
AGENCY FOR TOXIC SUBSTANCES AND DISEASE REGISTRY

Chemical and Physical Information

Chloroform

- Chloroform (also known as trichloromethane or methyl trichloride) is a volatile, colorless liquid with a pleasant, non-irritating odor and a slightly sweet taste.
- Chloroform is both a synthetic and naturally occurring compound. Natural production can occur through biotic and abiotic mechanisms in both aquatic and terrestrial environments, such as oceans, forest soils, grasslands, swamplands, peat moorlands, and rice fields. Additional natural sources include volcanic emissions and biomass burnings.
- Most of the chloroform produced by industry in the United States is used as a chemical intermediate, specifically for producing refrigerants and polymers used for non-corrosive, waterproof, or nonstick liners.
- Historically, chloroform was also used as an anesthetic during surgery, but it is no longer used for this purpose due to availability of safer alternatives.

Routes of Exposure

- Inhalation – Primary route of occupational exposure. The general population is also expected to be exposed to small amounts via inhalation of contaminated air.
- Oral – Primary route of exposure for the general population via ingestion of food and water containing chloroform.
- Dermal – Expected route of exposure for general population via direct contact with chloroform-containing water. Possible route of exposure for occupational population.

Chloroform in the Environment

- Chloroform can enter the environment from industrial facility waste streams or as a byproduct of water disinfection.
- In the atmosphere, it is expected to exist almost entirely in the vapor phase and can be removed by wet deposition.
- The dominant degradation of chloroform in the environment is its reaction with free radicals in the atmosphere.
- Its half-life in the atmosphere is on the order of months.
- Chloroform is expected to volatize rapidly from surface water.
- It does not adsorb significantly to soil or sediment and may therefore volatilize or migrate to groundwater.
- Chloroform does not significantly bioconcentrate in aquatic environments.

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

- A provisional acute-duration (≤14 days) inhalation MRL of 0.001 ppm (0.005 mg/m^3) was derived.
- A provisional intermediate-duration (15–364 days) inhalation MRL of 0.0008 ppm (0.004 mg/m^3) was derived.
- A provisional chronic-duration (≥365 days) inhalation MRL of 0.0004 ppm (0.002 mg/m^3) was derived.

Oral

- A provisional acute-duration (≤14 days) oral MRL of 0.3 mg/kg/day was derived.
- A provisional intermediate-duration (15–364 days) oral MRL of 0.1 mg/kg/day was derived.
- A provisional chronic-duration (≥365 days) oral MRL of 0.02 mg/kg/day was derived.

Health Effects

- In humans, depression of respiratory rates and respiratory arrest reported at high exposures are likely secondary to central nervous system (CNS) depression.
- The liver and kidney are targets of chloroform toxicity in humans following high-level inhalation or oral exposure.
- The nasal epithelium and underlying nasal bones appear to be the most sensitive targets in rodents following inhalation exposure.
- In animals, hepatic lesions (mild histopathological changes that progress to severe necrosis with high and/or long-term exposure) have been observed in inhalation and oral studies.
- Renal lesions have been seen in animals following inhalation and oral exposure.
- There is inconsistent evidence in humans and animals regarding developmental effects of chloroform exposure.
- The Department of Health and Human Services (HHS) determined that chloroform is reasonably anticipated to be a human carcinogen based on sufficient evidence in experimental animals. The U.S. Environmental Protection Agency (EPA) determined that chloroform is likely to be carcinogenic to humans under dose conditions that lead to cytotoxicity and regenerative hyperplasia in susceptible tissues; it is not likely to be carcinogenic by any route at dose levels that do not cause cytotoxicity and cell regeneration. The International Agency for Research on Cancer (IARC) determined that chloroform is possibly carcinogenic to humans based on inadequate evidence in humans and sufficient evidence in experimental animals.

Children's Health

- It is not known if children are more sensitive to chloroform exposure than adults.