ToxGuide™ for Chlorophenols

CAS # 95-57-8; 106-48-9; 576-24-9; 120-83-2; 583-78-8; 95-77-2; 591-35-5; 15950-66-0; 95-95-4; 88-06-2; 4901-51-3; 58-90-2; 935-95-5

June 2022

Sources of Exposure

General Populations

- Chlorophenols are used in the production of agriculture chemicals, pharmaceuticals, biocides, and dyes.
- The general population can be exposed to chlorophenols from ingestion of contaminated food and water or inhalation of contaminated air.
- The chlorophenols in this guide have rarely been detected in food items but have been shown to migrate from packaging materials used in some food containers.
- Small amounts of chlorophenols may be produced when water is disinfected with chlorine.
- Chlorophenols have been detected in children's wooden toys made in China.

Occupational Populations

- Occupational exposure to chlorophenols may occur through inhalation or dermal contact in facilities that produce or use these chemicals.

Toxicokinetics and Normal Human Levels

Toxicokinetics

- Chlorophenols are efficiently absorbed following inhalation, oral, and dermal exposure.
- Chlorophenols are widely distributed in the body, with the highest concentrations in the liver, kidney, and spleen. The extent of plasma protein binding, which is a major determinant of both the body burden and elimination kinetics, increases with increasing chlorine content.
- Rapid metabolism to glucuronide and sulfate conjugates appears to be the predominant route of chlorophenol metabolism. Metabolism of chlorophenols via cytochrome P-450 isozymes can also produce reactive quinone and semiquinone intermediates.
- Chlorophenols are rapidly excreted in the urine after oral, dermal, or intraperitoneal injection exposure. Half-lives in the range of hours to a few days have been estimated. Elimination rates tend to decrease with increasing chlorine content, likely due to increased plasma protein binding.

Normal Human Levels

- NHANES 2015–2016 reported the following geometric mean urinary concentrations: 0.596 μg/L for 2,4-dichlorophenol and 2.97 μg/L for 2,5-dichlorophenol. Geometric mean concentrations for 2,4,5-trichlorophenol and 2,4,6-trichlorophenol could not be calculated because the proportion of results below the lowest detectable level were too high to provide a valid result.

Biomarkers/Environmental Levels

Biomarkers

- There are no specific biomarkers for chlorophenols.
- Chlorophenols can be detected in urine, but exposure to other chemicals that are metabolized to chlorophenols will also result in chlorophenol in the urine.

Environmental Levels

Air

- There are no recent monitoring data for air levels of chlorophenols in the United States. A study from 1985 showed ambient air levels <2 ng/m^3 in Oregon.

Water

- There are no recent monitoring data for water levels of chlorophenols. Neither 2,4-dichlorophenol nor 2,4,6-trichlorophenol were detected in U.S. public water systems sampled between 2001 and 2005.

Sediment and Soil

- There are no recent monitoring data for levels of chlorophenols in the sediment or soil in the United States. 2-CP was not detected in sediment from Lake Michigan or the Susquehanna River Basin in the 1990s.

Reference

Agency for Toxic Substances and Disease Registry (ATSDR). 2022. Toxicological Profile for Chlorophenols. Atlanta, GA: U.S. Department of Health and Human Services, Public Health Services.

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

Chemical and Physical Information

Chlorophenols

- Chlorophenols are a group of chemicals in which the hydrogens on phenols (between 1 and 5) have been replaced with chlorines. There are 5 basic types of chlorophenols and 19 different chlorophenols. The following abbreviations will be used: chlorophenol (CP); dichlorophenol (DCP); trichlorophenol (TCP); and tetrachlorophenol (TeCP).
- Thirteen chlorophenols were evaluated for this guide. They include: 2-CP; 4-CP; 2,3-DCP; 2,4-DCP; 2,5-DCP; 3,4-DCP; 3,5-DCP; 2,3,4-TCP; 2,4,5-TCP; 2,4,6-TCP; 2,3,4,5-TeCP; 2,3,4,6-TeCP; and 2,3,5,6-TeCP.
- All of the chlorophenols evaluated are solid at room temperature except for 2-CP, which is liquid.
- Chlorophenols have a strong, medicinal smell. Small amounts can be tasted in water.
- Approximately 80–90% of chlorophenol use is for agricultural purposes. They have also been used in the production of pharmaceuticals, biocides, and dyes.
- Monochlorophenols are principally used as intermediates for production of higher chlorinated phenols. In the past, they were also used as antiseptics, but this is no longer common.

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 foodstuffs and water.
- Dermal – Likely route of exposure for occupational population.

Chlorophenols in the Environment

- Chlorophenols may enter the environment from industrial waste discharge, leaching from landfills, volatilization, application of pesticides, and chlorination of wastewater containing phenol.
- Under acidic conditions, chlorophenols have greater tendency to volatilize from water and adsorb to soil particles. Under neutral to alkaline conditions, volatilization from water and moist soils decreases and mobility in soils increases.
- Chlorophenols are considered moderately persistent. Resistance to biodegradation increases with increasing chlorine content and the location of the chlorine atoms on the aromatic ring.
- The chlorophenols in this guide are considered to possess low to moderate bioconcentration potential.
- Water contaminated through chlorination is most likely to contain lower chlorinated phenols, while higher chlorinated phenols are more likely to be found in fish.

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 chlorophenols.

Oral

- An acute-duration (≤14 days) oral MRL of 0.08 mg/kg/day was derived for 2,3,4,6-TeCP.
- Intermediate-duration (15–364 days) oral MRLs of 0.08 mg/kg/day (2-CP); 0.9 mg/kg/day (4-CP); 0.02 mg/kg/day (2,4-DCP); 1.0 mg/kg/day (2,4,5-TCP); 0.005 mg/kg/day (2,4,6-TCP) and 0.01 mg/kg/day (2,3,4,6-TeCP) were derived.
- No chronic-duration (≥365 days) oral MRL were derived for the chlorophenols.

Health Effects

- Neurological effects such as lethargy, tremors, convulsions, and/or central nervous system depression have been seen in humans after 2,4-DCP exposure. Similar effects were seen in animals exposed orally to 4-CP and 2,4-DCP or after a single dermal application of 2,3,4,5-, 2,3,4,6-, or 2,3,5,6-TeCP.
- Oral exposure to 2-DP, 4-CP, 2,4-DCP, 2,4,5-TCP, 2,4,6-TCP, and 2,3,4,6-TeCP in rats or mice led to increased liver weight, hepatocellular hypertrophy, and necrosis.
- Decreases in implantations, litter size, and/or live births per litter were reported in animals orally administered 4-CP, 2,4-DCP, and 2,4,6-TCP. Acute exposure to 2,4-DCP in mice led to a greater percentage of abnormal sperm and decreased sperm motility.
- Decreased body weight or body weight gain was seen after oral exposure to 2-CP, 4-CP, 2,4-DCP, 2,4,5-TCP, 2,4,6-TCP, and 2,3,4,6-TeCP in animals.
- Immune system effects were seen in rats exposed to 2,4-DCP.
- Association of chlorophenols to cancer in humans is complicated by the presence of other chemicals during exposure. Rats and mice exposed to 2,4,6-TCP in their diet had increased incidences of leukemia and liver cancer.
- 2,4,6-TCP has been classified by the U.S. Department of Health and Human Services as reasonably anticipated to be a human carcinogen, by the U.S. Environmental Protection Agency as probably carcinogenic to humans, and by the International Agency for Research on Cancer as possibly carcinogenic to humans.

Children's Health

- It is not known if children are more sensitive to chlorophenol exposure than adults, but neonatal rats are more susceptible to adverse effects after exposure to 2- and 4-CP than older rats.