United States Environmental Protection Agency | Pollution Prevention and Toxics (7407) | January 1995 EPA 749-F-95-007a

# OPPT Chemical Fact Sheets

## Chlorobenzene Fact Sheet: Support Document (CAS No. 108-90-7)

This summary is based on information retrieved from a systematic search limited to secondary sources (see Appendix A). These sources include online databases, unpublished EPA information, government publications, review documents, and standard reference materials. The literature search was done in January of 1995. No attempt has been made to verify information in these databases and secondary sources.

### I. CHEMICAL IDENTITY AND PHYSICAL/CHEMICAL PROPERTIES

The chemical identity and physical/chemical properties of chlorobenzene are summarized in Table 1.

**TABLE 1. CHEMICAL IDENTITY AND CHEMICAL/PHYSICAL PROPERTIES OF CHLOROBENZENE**

| Characteristic/Property | Data | Reference |
|---|---|---|
| CAS No. | 108-90-7 | |
| Common Synonyms | monochlorobenzene; benzene chloride MCB; chlorobenzol; Caswell No. 183A | ATSDR 1990 |
| Molecular Formula | $C_6H_5Cl$ | |
| Chemical Structure | | |
| Physical State | colorless liquid | ATSDR 1990 |
| Molecular Weight | 112.56 | ATSDR 1990 |
| Melting Point | -45.6°C | ATSDR 1990 |
| Boiling Point | 132°C | ATSDR 1990 |
| Water Solubility | 466.3 mg/L | U.S. EPA 1988 |
| Density | 1.1058 @ 20°C | ATSDR 1990 |
| Vapor Density (air = 1) | 3.9 | Keith and Walters 1985 |
| $K_{OC}$ | 126 | U.S. EPA 1988 |
| $K_{OW}$ | 692 | U.S. EPA 1988 |
| Vapor Pressure | 11.7 mm Hg @ 20°C | U.S. EPA 1988 |
| Reactivity | flammable | Keith and Walters 1985 |
| Flash Point | 29.4°C | ATSDR 1990 |
| Henry's Law Constant | $3.58 \times 10^{-3}$ atm·m$^3$/mol | ATSDR 1990 |
| Fish Bioconcentration Factor | 45.7 (rainbow trout); 446.7 (fathead minnow) | U.S. EPA 1988 |
| Odor Threshold | 0.05 mg/L (water); 1-8 mg/m$^3$ (air) | ATSDR 1990 |
| Conversion Factors | 1 ppm = 4.7 mg/m$^3$; 1 mg/m$^3$ = 0.22 ppm | ATSDR 1990 |

## II. PRODUCTION, USE, AND TRENDS

### A. PRODUCTION

In 1992, the United States production volume of chlorobenzene was 231 million pounds (USITC 1994). In 1984, the U.S. exported 41 million pounds of chlorobenzene (HSDB 1994). USITC (1994) and Mannsville (1990) have identified three U.S. producers of chlorobenzene, listed in Table 2 along with plant locations and production capacities.

**Table 2. U.S. PRODUCERS OF CHLOROBENZENE AND THEIR CAPACITIES**

| Producer | Plant Location | 1990 Capacity (Millions of Pounds) |
|---|---|---|
| Monsanto Company | Sauget, IL | 176 |
| PPG Industries, Inc. | Natrium, WV | 44 |
| Standard Chlorine Chemical Company of Delaware, Inc. | Delaware City, DE | 150 |
| TOTAL | | 370 |

Source: Mannsville 1990.

### B. USES

Chlorobenzene is used as a chemical intermediate in the production of ortho- and para-nitrochlorobenzenes. These chemicals are used as intermediates in the manufacture of rubber chemicals, agricultural chemicals, antioxidants, and dyes and pigments (Mannsville 1990). Chlorobenzene has also been used in the production of phenol; the insecticide DDT; and aniline (HSDB 1994) (see Table 3 for applicable SIC Codes). Chlorobenzene is also used as a solvent in the manufacture of adhesives, paints, polishes, waxes, diisocyanates, pharmaceuticals, and natural rubber (HSDB 1994; Sax and Lewis 1987; Windholz 1983). Other applications include use as a fiber swelling agent and dye carrier in textile processing; as a tar and grease remover in cleaning and degreasing operations; as a solvent in surface coating and surface coating removers; and as a heat-transfer medium (HSDB 1994).

**Table 3. END USE PATTERN OF CHLOROBENZENE--1989 ESTIMATE**

| Derivative (Typical Standard Industrial Classification (SIC) Code)[11] | Percentage of U.S. Use |
|---|---|
| Nitrochlorobenzenes (SIC 2865) | 40 |
| Solvents (SICs 2865, 2879) | 30 |
| Diphenol Ether and Phenylphenols (SIC 2865) | 15 |
| Sulfone Polymers (SIC 2865) | 5 |
| Miscellaneous (Various SICs) | 10 |
| TOTAL | 100 |

Source: Mannsville 1990.

## C. TRENDS

Over the past two decades, chlorobenzene has lost several of its U.S. markets, including the manufacture of phenol and aniline due to other, more efficient processes, and the manufacture of DDT, due to the ban on its domestic use. Over the next few years, overall demand for chlorobenzene is expected to remain flat (Mannsille 1990).

[1] The Standard Industrial Classification (SIC) code is the statistical classification standard for all Federal economic statistics. The code provides a convenient way to reference economic data on industries of interest to the researcher. SIC codes presented here are not intended to be an exhaustive listing; rather, the codes listed should provide an indication of where a chemical may be likely to be found in commerce.

## III. ENVIRONMENTAL FATE

### A. Environmental Release

There was no information in the secondary sources searched to indicate that chlorobenzene occurs naturally. Chlorobenzene enters the atmosphere as fugitive emissions from the pesticide industry and from other industries that use it as a solvent (Howard 1989). Release of the chemical also occurs during the disposal of industrial wastes (Howard 1989). Concentrations of chlorobenzene in the atmosphere have typically ranged from <0.02 ppb for remote areas to 0.8 ppb in cities; the maximum reported value measured was 12 ppb (Howard 1989).

Chlorobenzene was detected in the drinking water of several U.S. cities at concentrations of ≤5.6 ppb (micrograms/L). It was reported in ground water in 0.1% of 945 wells tested [at two sites, concentrations were 2.7 ppb and 14 ppt (nanograms/L)] and in surface water in 9.6% of the unspecified "large number" of samples tested (only 0.01% of the samples were >1 ppb; the maximum reported concentration was >10 ppb) (Howard 1989).

In 1992, environmental releases of chlorobenzene, as reported to the Toxic Release Inventory by certain types of U.S. industries, totaled about 2.3 million pounds, including 2.2 million pounds to the atmosphere, 72 thousand pounds to underground injection sites, 21 thousand pounds to surface water, and 817 pounds to land, (TRI92 1994).

### B. Transport

Chlorobenzene is volatile (vapor pressure, 11.7 mm Hg) and slightly soluble in water (466.3 mg/L) (ATSDR 1990; U.S. EPA 1988). Evaporation is an important transport process for the chemical from water and soil. Chlorobenzene evaporated from an unaerated aqueous solution at the rate of ≥99% in 72 hours (ATSDR 1990). The chemical may also adsorb moderately onto organic sediments ($K_{OC}$ of 126) (Howard 1989).

If released to moist soil, most of the chlorobenzene should volatilize to the atmosphere; if released to sandy soil, the chemical is mobile and is expected to leach into groundwater; it will biodegrade very slowly or not at all (Howard 1989). Under experimental conditions, chlorobenzene (1.04 mg/L) was added to a 140 cm deep soil column packed with sandy soil (Howard 1989). The fate of the chemical in the column was as follows: 27% volatilized, 23-33% percolated through the column, and 40-50% degraded or was not accounted for. At a chlorobenzene concentration of 0.18 mg/L, 54% volatilized, 26-34% percolated through the soil column, and 12-20% degraded or was not accounted for (Howard 1989). The time-span of this experiment was not reported.

## C. Transformation/Persistence

1. Air — One source estimated the half-life of chlorobenzene in air to be about 9 days (U.S. EPA 1988); another source estimated the half-life to be 20 to 40 hours under simulated atmospheric conditions (ATSDR 1990). The predominant removal mechanism for chlorobenzene in the atmosphere is the reaction with photochemically generated hydroxyl radicals (U.S. EPA 1988). Chlorobenzene absorbs light in the 290-310 nm region, suggesting photolysis as an additional, but slow, mechanism of degradation, resulting in the production of monochlorobiphenyl (Howard 1989). In the atmosphere, photolysis would occur over the course of a month (Howard 1989).

2. Water — The main fate processes for chlorobenzene in water are vaporization and biodegradation (U.S. EPA 1988; Howard 1989). Reported half-lives of chlorobenzene in water are 0.3 days in a river (U.S. EPA 1988); about 1 to 12 hours in a rapidly flowing stream (Howard 1989); and 75 days in sediment in an estuarine river under near natural conditions (Howard 1989). Biodegradation will occur in warm weather, particularly with acclimated microorganisms, proceeding more rapidly in fresh water than in estuarine and marine systems (Howard 1989). The biodegradation half-life of chlorobenzene was 150 days in river water and 75 days in sediment (Howard 1989). Direct photolysis is not a significant process for the removal of chlorobenzene from surface water (half-life, ~170 years in summer at 40° latitude) (Howard 1989).

3. Soil — Evaporation is expected to be the main removal process for chlorobenzene at the soil surface (U.S. EPA 1988). Over the course of one day, chlorobenzene applied to soil at the concentration of 1 kg/ha at depths of 1 cm and 10 cm disappeared at the rate of 86.5 and 23.4%, respectively (Howard 1989). Based on these data, the volatilization half-lives were estimated to be 0.3 and 12.6 days, respectively (Howard 1989). Chlorobenzene may adsorb to organics in soil and, if retained long enough, may undergo biodegradation. Acclimation of the microorganisms is important in the biodegradation of chlorobenzene (Howard 1989). Twenty percent mineralization in a week was reported in one study; the main products of biodegradation are 2- and 4-chlorophenol (Howard 1989).

4. Biota — The bioconcentration factors for chlorobenzene (45.7, rainbow trout; 446.7, fathead minnow) and the chemical's octanol/water partition coefficient (692) (U.S. EPA 1988), suggest a some potential for bioconcentration. Howard (1989) predicts little or no bioconcentration for chlorobenzene.

## IV. HEALTH EFFECTS

### A. Pharmacokinetics

1. Absorption — Reports of toxic effects in humans following ingestion or inhalation of chlorobenzene indicate that the chemical is absorbed by these routes (U.S. EPA 1988). In one study, a human volunteer absorbed about 31% of orally administered chlorobenzene (ATSDR 1990). Rats given chlorobenzene orally absorbed 18% to 22% of the dose. Absorption of chlorobenzene from the gastrointestinal tract is facilitated by the ingestion of fats and oils (U.S. EPA 1988).

   Two workers exposed to 0.84 and 0.5 ppm of chlorobenzene by inhalation absorbed 38 and 45%, respectively, of the administered dose (ATSDR 1990). Rats inhaling $^{14}$C-labeled chlorobenzene readily absorbed concentrations up to 700 ppm (ATSDR 1990).

   No information was found regarding the dermal absorption of chlorobenzene. However, a report of "signs of toxicity" in rats following skin application of high doses of chlorobenzene (ACGIH 1991) suggests dermal absorption of the chemical.

2. Distribution — In rats exposed by inhalation to $^{14}$C-labeled chlorobenzene in single or multiple 8-hour exposures, the chemical was distributed preferentially to the epididymal and perirenal adipose tissue (ATSDR 1990). The amount of the label in fat tissue increased 8 to 10 times when the concentration of chlorobenzene was increased from 100 to 400 ppm and 3 to 5 times when the concentration was increased from 400 to 700 ppm. In the remainder of the tissues (which were not identified), the radioactivity increased in proportion to the exposure concentration.

3. Metabolism — Chlorobenzene is oxidized to the intermediate, 4-chlorobenzene-1,2-epoxide (ATSDR 1990). The epoxide undergoes glutathione conjugation, hydrolysis, or transition to form p-chlorophenylmercapturic acid, 4-chlorocatechol, or 4-chlorophenol, respectively. p-Chlorophenylmercapturic acid and 4-chlorocatechol, the main metabolites, were detected in the urine of humans exposed to chlorobenzene orally or by inhalation, and in the urine of rats following oral administration of the chemical (ATSDR 1990).

4. Excretion — The major routes for the excretion of chlorobenzene are in the urine as metabolites (see section IV.A.3) and in expired air, mainly unchanged (ATSDR 1990). For two workers exposed to 0.84 and 0.5 ppm of chlorobenzene in air, the excretion of *p*-chlorophenylmercapturic acid was significantly lower than that of 4-chlorocatechol; however, the ratios of *p*-chlorophenylmercapturic acid to 4-chlorocatechol were similar for subjects exposed either orally or by inhalation (ATSDR 1990). The respiratory elimination of radiolabel by rats exposed for 8 hours to $^{14}$C-chlorobenzene vapor concentrations ranging from 100 to 700 ppm indicated a two compartment elimination (ATSDR 1990). Rabbits given oral doses of $^{14}$C-labeled chlorobenzene excreted 22% of the label in the urine and the remainder in expired air (ATSDR 1990).

**B. Acute Effects**

Chlorobenzene can be irritating to the eyes and respiratory tract of humans. In animals, the chemical is moderately irritating to the eyes and skin. Chlorobenzene has low to moderate systemic toxicity in animals, causing death at moderate to high oral doses and at high inhalation concentrations.

1. Humans — A 70-year-old woman, exposed over a period of 6 years (frequency of exposure not specified) to a glue containing 70% chlorobenzene, experienced headaches and irritation of the upper respiratory tract and eyes from the onset of exposure (U.S. EPA 1988).

2. Animals — Oral $LD_{50}$ values of chlorobenzene are 400 to 1600 mg/kg for rats and 2830 mg/kg for rabbits (ACGIH 1991). Inhalation $LC_{50}$ values for chlorobenzene are 12,000 ppm (30 minutes) in the rat and 8,000 ppm (30 minutes) in the cat (Verschueren 1983). Exposure of rats by inhalation to 22,000 ppm killed two of three animals in 2.3 hours; at 9000 ppm two of three animals died within 3 hours (ACGIH 1991). Doses of 10 mL/kg applied to the skin of guinea pigs were nonlethal (ACGIH 1991). Rats given single dermal applications of $\geq$3600 mg/kg of chlorobenzene exhibited unspecified signs of toxicity (ACGIH 1991).

   Chlorobenzene is a moderate skin irritant in the guinea pig and a moderate eye irritant in the rabbit (ACGIH 1991).

**C. Subchronic/Chronic Effects**

EPA has derived a chronic oral reference dose RfD[2] of 0.02 mg/kg/day for chlorobenzene, based on histopathologic changes in the liver of dogs. High doses of chlorobenzene administered to animals orally or by inhalation produced adverse effects on body weight, liver, kidney, bone marrow, and nervous system (see section IV.G.). A single case study reported aplastic bone marrow resulting from exposure of a worker to chlorobenzene.

1. Humans — A 70-year-old woman, exposed over a period of 6 years (frequency of exposure not specified) to a glue containing 70% chlorobenzene developed aplastic bone marrow (U.S. EPA 1988).

2. Animals — EPA has derived a chronic oral RfD for chlorobenzene of 0.02 mg/kg/day, based on histopathologic changes in the liver of dogs treated with the chemical for 13 weeks (U.S. EPA 1994). Male and female beagle dogs received chlorobenzene doses of 27.25, 54.5, or 272.5 mg/kg/day in capsules, 5 days/week for 13 weeks. The animals given 54.5 mg/kg/day [the LOAEL (lowest-observed-adverse-effect level)] exhibited liver changes that included slight bile duct proliferation, cytologic alterations, and leukocytic infiltration of the stroma. At the highest dose, the effects were more severe and included death; body weight loss; changes in hematology, clinical chemistry, and urine composition; and pathologic changes in the liver, kidney, gastrointestinal mucosa, and hematopoietic tissue (U.S. EPA 1994). The NOAEL (no-observed-adverse-effect level) for the study was 27.25 mg/kg/day.

   In other studies, subchronic or chronic administration of chlorobenzene produced the following adverse effects in animals: (1) increased liver and kidney weights in rats given 100 mg/kg/day in a 90-day feeding study (NOAEL, 50 mg/kg/day); (2) liver histopathology in rats given 144 mg/kg/day in a 6-month gavage study (NOAEL, 14.4 mg/kg/day); (3) increased liver weights in rats and mice given 125 mg/kg/day in 90-day gavage studies (NOAEL for both species, 60 mg/kg/day); and (4) liver histopathology in rats and mice given 120 mg/kg/day in 2-year gavage studies (NOAEL for both species, 60 mg/kg/day) (U.S. EPA 1994).

   Higher oral doses of chlorobenzene, 500 and 750 mg/kg/day administered to rats for 13

[2] The RfD is an estimate (with uncertainty spanning perhaps an order of magnitude) of the daily exposure level for the human population, including sensitive subpopulations, that is likely to be without an appreciable risk of deleterious effects during the time period of concern.

weeks, caused decreased body weight gain, increased enzyme levels, increased excretion of porphyrins, liver necrosis, nephropathy, and myeloid depletion of bone marrow. Animals given 750 mg/kg/day also exhibited higher mortality and lymphoid depletion in the thymus and spleen (U.S. EPA 1988). Mice given doses of $\geq$250 mg/kg for 13 weeks had decreased body weight gain, decreased survival, dose-dependent hepatocellular necrosis, nephropathy, thymic necrosis and lymphoid or myeloid depletion of the thymus, spleen and bone marrow.

Inhalation exposure of animals to chlorobenzene produced the following effects: hepatomegaly and histopathological changes (rats, 475 ppm 7 hours/day, 5 days/week for 44 days); liver necrosis and regeneration; kidney hyperplasia and pneumonia (0.021 or 0.21 ppm, continuously for 72-80 days); focal lesions in adrenal cortex and kidney tubules, congestion of liver and kidney, decreased SGOT (rats, 75 ppm, 7 hours/day, 5 days/week for 120 days) (U.S. EPA 1988). Other studies reported no effects in rats exposed to 425 ppm, 6 hours/day, 5 days/week for 87 days and in rabbits and guinea pigs exposed to 200 ppm, 7 hours/day, 5 days/week for 44 days (U.S. EPA 1988). The concentrations of 0.021 ppm (the lowest effective concentration with continuous exposure) and 475 ppm (the highest concentration producing no effect with intermittent exposure) convert to doses of 0.06 and 228 mg/kg/day, respectively (U.S. EPA 1988).

## D. Carcinogenicity

Based on cancer information in humans, equivocal animal data, and predominantly negative genetic toxicity information (see Section IV.E), the EPA has classified chlorobenzene as a Group D; it is not classifiable as to human carcinogenicity potential.

1. Humans — No information was found in the secondary sources searched regarding the carcinogenicity of chlorobenzene in humans.

2. Animals — In an NTP bioassay, male and female F344/N rats and female B6C3$F_1$ mice (50/sex/dose) were given chlorobenzene doses of 60 or 120 mg/kg/day by gavage, 5 days/week for 103 weeks; male B6C3$F_1$ mice received 30 or 60 mg/kg/day (NTP 1985; U.S. EPA 1994). Increased mortality was statistically significant for male rats (P=0.033, high dose), but not for female rats and mice and male mice (NTP 1985; U.S. EPA 1994). A statistically significant positive trend in the incidence of hepatocellular neoplastic nodules was observed in male rats (4/50, 2/50, 4/49, and 8/49 for untreated controls, vehicle controls, low-dose, and high dose groups, respectively). There were no increases in hepatocellular neoplastic nodules for female rats and male and female mice, and there were no increases in hepatocellular or other site-specific tumors for male and female rats and mice. The NTP concluded that "under the conditions of these studies, chlorobenzene administration increased the occurrence of neoplastic nodules of the liver in high-dose male F344/N rats, providing some, but not clear evidence of carcinogenicity of chlorobenzene in male rats. Carcinogenic effects of chlorobenzene were not observed in female F344/N rats or in male or female B6C3$F_1$ mice" (NTP 1985). Based on no human data, inadequate animal data and predominantly negative genetic toxicity data, the EPA has classified chlorobenzene as D, not classifiable as to human carcinogenicity (U.S. EPA 1994). Note that this bioassay meets earlier NCI guidelines but not current NTP or TSCA guidelines.

## E. Genotoxicity

The genotoxicity information for chlorobenzene is mostly negative. It is not adequate to support a concern for mutagenicity or for carcinogenicity for MCB.

Results of unscheduled DNA synthesis testing on monochlorobenzene have been voluntarily submitted to EPA. Rat cells were exposed *in vitro* to the following percent volume to volume concentrations of MCB: $10^{-1}$, $10^{-2}$, $10^{-3}$, $10^{-4}$. Cytotoxicity was observed at all concentrations. Chlorobenzene did not induce DNA repair at any concentration.

Chlorobenzene was negative for genotoxicity in *Salmonella typhimurium* strains TA98, TA100,

TA1535, TA1537 or TA1538 with or without metabolic activation; did not induce DNA damage in *Escherichia coli* strains WP2 uvr A+ rec A+ or WP100 uvr A- rec A- or *S. typhimurium* strains TA1978 uvr B+ or TA1538 uvr B- (U.S. EPA 1994). The chemical was also negative for the induction of specific locus forward mutations in mouse lymphoma L5178Y cells, both with and without metabolic activation.

Chlorobenzene treatment increased the number of revertants in *Actinomycetes antibioticus*-400 and *Aspergillus nidulans* and caused mitotic disturbances in *Allium cepa* (U.S. EPA 1994). The chemical induced reciprocal recombination in *Saccharomyces cerevasiae* strain D3 with metabolic activation (U.S. EPA 1994).

## F. Developmental/Reproductive Toxicity

The chlorinated benzene industry has submitted to EPA results of a 2-generation reproductive effects study on MCB. Results show that testicular damage occurred in rats exposed by inhalation to MCB concentrations as low as 150 ppm. The no-observed-effect level in the study was 50 ppm.

1. Humans — No information was found in the secondary sources searched regarding the developmental/reproductive toxicity of chlorobenzene in humans.

2. Animals — Pregnant Fischer 344/N rats and New Zealand rabbits (30-33 animals/group) were exposed by inhalation to 0, 75, 210, or 590 ppm of chlorobenzene for 6 hours/day on days 6-15 of gestation (rats) or days 6-18 of gestation (rabbits). Maternal toxicity was evident in the rats exposed to 590 ppm. The fetuses of the animals of this group had delayed ossification of the vertebral centra and bilobed thoracic centra, indicative of a slight delay in skeletal development that was possibly related to the maternal toxicity. No other signs of developmental toxicity were observed (John et al., 1984). The rabbits exposed to 210 and 590 ppm also displayed signs of maternal toxicity. External and visceral malformations occurred among the exposed fetuses, but these effects were neither dose-related nor consistent in type. A repeat study using concentrations of chlorobenzene up to 590 ppm did not reveal any significant increase or trend for clustering of malformations in the exposed groups, although there were signs of maternal toxicity at the higher concentrations.

   EPA issued a final rule under Section 4 of the Toxic Substances Control Act requiring manufacturers and processors of monochlorobenzene to conduct testing for reproductive and fertility effects of MCB in rats exposed by inhalation. The study appears to have been well conducted (U.S. EPA 1986a). Male and female Sprague-Dawley rats (30/sex/group) were exposed to chlorobenzene concentrations of 0, 50, 150, or 450 ppm 6 hours/day, 7 days/week for 10 weeks prior to mating, and during mating, gestation, and lactation (females were not exposed during days 1-5 of lactation). Beginning 1 week after weaning, both sexes from the $F_1$ generation received the same treatment as the $F_0$ generation. The observed effects included:

   - Increased relative liver weights in $F_0$ and $F_1$ rats of both sexes in the mid- and high-concentration groups, and in $F_1$ males exposed to 50 ppm;
   - Decreased survival index for the pups in the high-concentration, $F_2$ litters;
   - Increased incidences of dilated renal pelvis and small flaccid testes in high-concentration $F_0$ and $F_1$ adults; and
   - Increased incidences of hepatocellular hypertrophy, renal degeneration and inflammation, and bilateral degeneration of the germinal epithelium of the testes in male $F_0$ and $F_1$ rats exposed to the mid and high concentrations.

   The lowest-observed-effect level for adverse reproductive effects of MCB in this study was 150 ppm. The no-observed-effect level in this study was 50 ppm. Results of these studies provide sufficient information to conclude that MCB has potential to produce adverse

reproductive effects in human males (U.S. EPA 1986a).

In an inhalation study, 2 of 4 dogs exposed to 434 ppm, 6 hours/day, 5 days/week for 62 exposures had bilateral atrophy of the germinal epithelium of the seminiferous tubules. This effect was not observed in dogs exposed to 319 ppm (U.S. Air Force 1989).

Three of four male dogs given 272.5 mg/kg/day of chlorobenzene orally for 13 weeks exhibited decreased spermatogenesis and tubular atrophy; this dose also caused an unspecified number of deaths or moribundity (U.S. Air Force 1989).

### G. Neurotoxicity

Chlorobenzene can cause neurotoxic effects in humans in cases where exposure occurs either orally or by inhalation. Symptoms of acute exposure to large amounts of chlorobenzene include unconsciousness and cyanosis. Chronic exposure can cause headaches, drowsiness, numbness of the extremities, and spastic contractions of the muscles. Animals exhibited narcosis and muscle spasms following acute exposure to high concentrations, and neuromuscular disorders following continuous exposure to low concentrations.

1. Humans — A two-year-old male who swallowed 5 to 10 cc (0.53-1.06 g/kg for a 10 kg child) of a stain remover consisting almost entirely of chlorobenzene became unconscious, did not respond to skin stimuli, had muscle spasms, and was cyanotic; the odor of chlorobenzene was apparent in his urine and exhaled air. The child recovered uneventfully (ATSDR 1990).

   Factory workers (n=28) reportedly exposed to chlorobenzene via inhalation for 1-2 years (details of exposure not specified) experienced headaches; somnolence; dyspepsia; tingling, numbness, and stiffness of the extremities (8 workers); hyperesthesia of the hands (4 workers); and spastic contractions of the finger muscles (9 workers) or of the gastrocnemius (2 workers) (U.S. EPA 1988). In another survey, workers (n=26) exposed to chlorobenzene alone or to a combination of benzene and chlorobenzene for <1 year (study details not provided) showed no signs of neurotoxicity (U.S. EPA 1988).

2. Animals — Rats and mice exposed to chlorobenzene concentrations of 5,850 ppm for 30 minutes by inhalation exhibited central nervous system depression, whereas animals exposed to 2,990 ppm were not sedated (ACGIH 1991). Narcosis was observed in animals inhaling 1,200 ppm chlorobenzene for 2 hours, but narcosis was not observed in animals inhaling 220-660 ppm (ACGIH 1991). Rabbits exposed by inhalation to $\geq$1,090 ppm chlorobenzene for 2 hours exhibited muscle spasms followed by narcosis (ATSDR 1990).

   Subchronic or chronic inhalation exposure of rats to chlorobenzene produced the following effects: encephalopathy (0.021 or 0.21 ppm, continuously for 72-80 days); inhibition of chronaxia of antagonistic muscles and increased blood cholinesterase (rats, 0.21 ppm continuously for 60 days); and chronaximetric inhibition (21 ppm for 49-98 days). Information was identified in a table presented in U.S.EPA 1988. The subject studies were not addressed in the text and no additional information is available. No conclusions were drawn as regards the reversibility of the effects seen or the overall significance of these studies. In addition, due to the absence of corroborating evidence from domestic literature, the information is not considered reliable for use in risk assessment (U.S. EPA 1988).

## V. ENVIRONMENTAL EFFECTS

Chlorobenzene is moderately toxic to aquatic organisms with toxicity values in the range between >1 mg/L to 100 mg/L. Chlorobenzene is not expected to be toxic to aquatic or terrestrial animals at levels normally found in the U.S. environment.

### A. Toxicity to Aquatic Organisms

Threshold limit values for chlorobenzene in fish exposed for 24 to 96 hours are as follows: 29-39 mg/L for the fathead minnow (*Pimephales promelas*); 24 mg/L for the bluegill (*Lepomis macrochirus*); 51-73 mg/L for the goldfish (*Carassius auratus*); and 45 mg/L for the guppy (*Poecilia reticulata*) (Verschueren 1983). The 24-hour $LD_{50}$ is 1.8 mL/L for the rainbow trout and the 14-day $LC_{50}$ is 19 mg/L for the guppy (Verschueren 1983). Toxicity threshold values for the cell multiplication inhibition test are as follows: 17 mg/L for bacteria (*Pseudomonas putida*); 120 mg/L for algae (*Microcystis aeruginosa*); and an EC3 >390 mg/L for green algae (*Scenedesmus quadricauda*); and >390 mg/L for protozoa (*Entosiphon sulcatum*) (Verschueren 1983). An algal 96-h EC50 of 8.9 mg/L is predicted for chlorobenzene using the neutral organic quantitative structure activity relationship (QSAR) (Clements et al.,1986). In the absence of daphnid data, a 48-h EC50 daphnid value of 13.6 mg/L is predicted for chlorobenzene using the neutral organic QSAR (Clements et al., 1986).

### B. Toxicity to Terrestrial Organisms

No information was found in the secondary sources searched regarding the toxicity of chlorobenzene to terrestrial organisms. However, the acute toxicity values for laboratory rats [oral $LD_{50}$, 400 to 1600 mg/kg (ACGIH 1991); inhalation $LC_{50}$, 12,000 ppm for 30 minutes (Verschueren 1983)] indicate that the chemical would not be toxic to terrestrial animals at levels expected to be present in the U.S. environment.

### C. Abiotic Effects

No information was found in the secondary sources searched regarding the abiotic effects of chlorobenzene.

## VI. EPA/OTHER FEDERAL/OTHER GROUP ACTIVITY

The Clean Air Act Amendments of 1990 list chlorobenzene as a hazardous air pollutant. Chlorobenzene has been included in the first Toxic Substance Control Act ( TSCA) section 4 proposed test rule for hazardous air pollutants for the following tests: acute effects, subchronic inhalation toxicity, neurotoxicity, and immunotoxicity. Occupational exposure to chlorobenzene is regulated by the Occupational Safety and Health Administration (OSHA). The OSHA permissible exposure limit (PEL) is 75 parts per million of air (ppm) as an 8-hour time-weighted average (TWA) (29 CFR 1910.000). In addition to OSHA, other federal agencies and groups may develop recommendations to assist in controlling workplace exposure. These agencies and groups (listed in Tables 4 and 5) should be contacted regarding workplace exposures and for additional information on chlorobenzene.

**TABLE 4. EPA OFFICES AND CONTACT NUMBERS INFORMATION ON CHLOROBENZENE**

| EPA Office | Statute | Contact Number |
|---|---|---|
| Pollution Prevention & Toxics | PPA[a] | (202) 260-1023 |
| | EPCRA (§313/TRI)[b] | (800) 535-0202 |
| | TSCA (§4, §8A, §8D)[c] | (800) 554-1404 |
| Air | Clean Air Act (§111, §112B)[d] | (919) 541-0888 |
| Solid Waste & Emergency Response | RCRA (Action levels: 20 µg/$m^3$, air 0.7 mg/L, water 2000 mg/kg, soil)[e] | (800) 535-0202 |
| | CERCLA (RQ, 100 pounds)[f] | (800) 535-0202 |
| Water | Clean Water Act (§304b, §307a, §311) | (202) 260-7588 |
| | WQC (680 µg/L [ao/do]; 21,000 µg/L [ao]) | |
| | Safe Drinking Water Act (MCLG: 0.1 mg/L; MCL: 0.1 mg/L)[g] | (800) 426-4791 |
| | Health Advisories (2 mg/L [ch/1d, ch/10d, ch/lt]; 7 mg/L [a/lt]; 0.1 mg/L [a/lifetime])[h] | |

[a]**PPA**: Pollution Prevention Act

[b]**EPCRA**: Emergency Planning and Community Right to Know Act of 1986

[c]**TSCA**: Toxic Substances Control Act

[d]Listed as hazardous air pollutant under § 112 of Clean Air Act [42 U.S.C. 7401 et seq.]

[e]**RCRA**: Resource Conservation and Recovery Act (40 CFR 264.94). **Action Level**: Health and environmental-based levels used by the EPA as indicators for the protection of human health and the environment and as triggers for a Corrective Measure Study.

[f]**CERCLA**: Comprehensive Environmental Response, Compensation, and Liability Act of 1980, as amended. **RQ**: level of hazardous substance, which, if equaled or exceeded in a spill or release, necessitates the immediate reporting of that release to the National Response Center (40 CFR Part 302).

[g]**MCL** (Maximum Contaminant Level): promulgated pursuant to the Safe Drinking Water Act [40 CFR Part 141 (1994)]. **MCLG** (Maximum Contaminant Level Goal): a non-enforceable concentration of a drinking water contaminant that is protective of adverse human health effects and allows an adequate margin of safety.

[h]**Drinking Water Health Advisories**: estimated for a 10-kg child consuming 1 L of water per day or a 70-kg adult consuming 2 L of water per day. **(ch/1d)** (one-day health advisory for a child): the concentration of a chemical in drinking water that is not expected to cause any adverse noncarcinogenic effects for up to 5 consecutive days of exposure, with a margin of safety. **(ch/10d)** (for a child): the concentration of a chemical in drinking water that is not expected to cause any adverse noncarcinogenic effects up to 14 consecutive days of exposure, with a margin of safety. **(ch/lt)** (child, long-term health advisory): the concentration of a chemical in drinking water that is not expected to cause any adverse noncarcinogenic effects up to approximately 7 yr (10% of an individual's lifetime) of exposure, with a margin of safety. **(a/lt)**: adult, long-term health advisory; may cover several months to several years. **lifetime** (lifetime health advisory): the concentration of a chemical in drinking water that is not expected to cause any adverse noncarcinogenic effects over a lifetime of exposure, with a margin of safety.

[i]WQC: Federal ambient water quality criteria for the protection of human health (56 FR 58420). **Ambient Water Quality Criteria standards**: established pursuant to the Clean Water Act, 57 FR 60848, December 22, 1992. **(ao/dw)**: protection for consuming aquatic organisms and drinking water; (ao): protection for consuming aquatic organisms.

**TABLE 5. OTHER FEDERAL OFFICES/CONTACT NUMBERS FOR INFORMATION ON CHLOROBENZENE**

| Other Agency/Department/Group | Contact Number |
|---|---|
| Agency of Toxic Substances & Disease Registry | (404) 639-6000 |
| American Conference of Governmental Industrial Hygienists (TLV-TWA, 10 ppm)[a] | (513) 742-2020 |
| Consumer Product Safety Commission | (301) 504-0994 |
| Food & Drug Administration | (301) 443-3170 |
| National Institute for Occupational Safety & Health (TWA, not established; IDLH, 2400 ppm)[b] | (800) 356-4674 |
| Occupational Safety & Health Administration (TWA, 75 ppm)[c] Check local phone book for phone number under Department of Labor | |

[a]TLV-TWA: Time-weighted-average concentration for a normal 8-hour workday and a 40-hour workweek to which nearly all workers may be repeatedly exposed without adverse effects (ACGIH 1993-1994).

[b]IDLH: Immediately dangerous to life or health (NIOSH 1990; 1992).

[c]TWA: Time-weighted-average that must not be exceeded during any 8-hour work shift of a 40-hour workweek. Standard promulgated pursuant to the Occupational Safety and Health Act, 29 CFR 1910 (OSHA 1993).

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