CHLOROBENZENE

CAS number:	108-90-7
Synonyms:	Monochlorobenzene, benzene chloride, chlorobenzol, phenyl chloride
Chemical formula:	C_6H_5Cl
Structural formula:	—

Workplace exposure standard (amended)

TWA:	**5 ppm (23 mg/m^3)**
STEL:	**—**
Peak limitation:	**—**
Notations:	**—**
IDLH:	**1,000 ppm**
Sampling and analysis:	The recommended value is quantifiable through available sampling and analysis techniques.

Recommendation and basis for workplace exposure standard

A TWA of 5 ppm (23 mg/m^3) is recommended to protect for liver effects in exposed workers.

There are no acute effects reported within ten times of the TWA and the TWA is considered protective for any short-term effects. Therefore, a STEL is not recommended.

Discussion and conclusions

Chlorobenzene is used as a chemical intermediate, a heat transfer medium and as a solvent. It has the potential to cause liver changes including congestion and increasing weight (ACGIH, 2018).

Limited toxicological data are available in humans. An industrial case study noted that workers exposed to an unknown concentration of chlorobenzene reported headaches, respiratory and eye irritation (ACGIH, 2018).

A multi-generational, inhalation study in rats identified a LOAEL at 50 ppm for liver weight increase and kidney changes (SCOEL, 2003). The recommended TWA of 5 ppm is derived using the reported LOAEL of 50 ppm and application of an uncertainty factor of 10 to allow for intra- and interspecies variation and for the absence of a NOAEL. Based on the above, the recommended TWA is considered sufficiently low to minimise the potential for liver and kidney effects in exposed workers.

Recommendation for notations

Not classified as a carcinogen according to the Globally Harmonized System of Classification and Labelling of Chemicals (GHS).

Not classified as a skin sensitiser or respiratory sensitiser according to the GHS.

A skin notation is not recommended based on available data.

APPENDIX

Primary sources with reports

Source	Year set	Standard
SWA	***1991***	***TWA: 10 ppm (46 mg/m^3)***
ACGIH	***2001***	***TLV-TWA: 10 ppm (46 mg/m^3)***

TLV-TWA recommended to minimise the potential for liver changes including congestion and increasing weight.

Summary of data:

Human data:

- Odour threshold 0.21 ppm
- Workers exposed to an unknown concentration in a glue preparation reported headaches, respiratory and eye irritation
- Case report of myeloproliferative lesions developing in workers exposed to a mixture with ortho-dichlorobenzene and trichlorobenzene; no further information.

Animal data:

- LD_{50}: 400–1,600 mg/kg (rats, oral), 2,830 mg/kg (rabbits, oral)
- LOAEL: 3,600 mg/kg (rats, dermal)
- Rabbits, rats and guinea pigs exposed to a vapour/aerosol mix of 4 mg/L (≈850 ppm) combined with 1 mg/L dichlorobenzene (≈166 ppm) developed eye, mucus irritation and weight loss
- Rabbits, rats and guinea pigs exposed at 1,000 ppm (7 h/d, 5 d/wk, 44 d) developed lung, liver and kidney changes, NOEL: 200 ppm
- Rabbits and rats (male) exposed at 0, 75, 200 ppm (7 h/d, 5 d/wk, 24 wk):
  - rabbits: decrease in serum glutamic-oxaloacetic transaminase
  - rats: decrease in serum glutamic-oxaloacetic transaminase, microcytic anaemia, increased liver weight, lesions to the kidney and adrenal cortex and congestion in the liver and kidney
- Rabbits and rats (male) exposed at 0, 50, 150, 450 ppm (2 generations); no adverse reproductive effect but liver weight increased in generation F_1 males at 50 ppm
- Increased frequency of neoplastic nodules of the liver at 120 mg/kg (rats, mice; oral)
- Negative results in mutagenicity assays.

DFG	***1999***	***MAK: 10 ppm (47 mg/m^3)***

Summary of additional data:

- 4 men exposed for 7 h at 60.2 ppm (3 h, 1 h pause, 4 h) reported symptoms including sleepiness, headaches, pulsating pain in the eyes and dry throat
- Multi-generation study in rats identified liver weight increases in male rats of the F_1 generation exposed at 50 ppm; kidney changes (interstitial nephritis, focal epithelial regeneration) also noted at 50 ppm
- Rats exposed at 75 ppm for 11 weeks developed increased liver weights and histopathological changes in the kidneys
- Previous MAK of 50 ppm reduced due to evidence in animals presented above.

Source	Year set	Standard
SCOEL	***2003***	***TWA: 5 ppm (23 mg/m^3); STEL: 15 ppm (70 mg/m^3)***
Summary of additional data: • LOAEL of 50 ppm identified in two-generation rat inhalation study; increased liver weights and adverse kidney effects (same as DFG, 1999) • TWA calculated by applying an uncertainty factor of 10 to allow for intra- and interspecies variation and for the absence of a NOAEL in the selected 2 generation rat study.		
OARS/AIHA	***NA***	***NA***
No report.		
HCOTN	***NA***	***NA***
No report.		

Secondary source reports relied upon

Source		Year	Additional information
HSE	✓	2008	• TWA: 1 ppm; STEL: 3 ppm • Skin notation assigned • Toxicological data do not identify clear positive evidence for serious effects on human health at 1 ppm or 5 ppm • Exposure data demonstrate that control to <5 ppm (8 h TWA) is reasonably practicable and that most results are below 1 ppm.
NICNAS	✓	2016	• No additional information.
ECHA	✓	2013	• LC_{50}: ≈3,000 ppm in 2 rat studies.

Carcinogenicity — non-threshold based genotoxic carcinogens

Is the chemical mutagenic? No

The chemical is not a non-threshold based genotoxic carcinogen.

Notations

Source	Notations
SWA	NA
HCIS	NA
NICNAS	NA
EU Annex	NA
ECHA	NA
ACGIH	Carcinogenicity – A3
DFG	NA
SCOEL	NA

Source	Notations
HCOTN	NA
IARC	NA
US NIOSH	NA

NA = not applicable (a recommendation has not been made by this Agency); — = the Agency has assessed available data for this chemical but has not recommended any notations

Skin notation assessment

Calculation	
Adverse effects in human case study:	no
Dermal LD_{50} ≤1000 mg/kg:	no
Dermal repeat-dose NOAEL ≤200 mg/kg:	
Dermal LD_{50}/Inhalation LD_{50} <10:	
In vivo dermal absorption rate >10%:	
Estimated dermal exposure at WES >10%:	
	a skin notation is not warranted

A dermal LD_{50} was not determined, however based on the LOAEL of 3,600 mg/kg (rats, dermal) it is presumed the LD_{50} would be <1,000 mg/kg

IDLH

Is there a suitable IDLH value available?	Yes

Additional information

Molecular weight:	112.56
Conversion factors at 25°C and 101.3 kPa:	1 ppm = 4.6 mg/m^3; 1 mg/m^3 = 0.2 ppm
This chemical is used as a pesticide:	☐
This chemical is a biological product:	☐
This chemical is a by-product of a process:	☐
A biological exposure index has been recommended by these agencies:	✓ ACGIH ✓ DFG ☐ SCOEL

Workplace exposure standard history

Year	Standard
Click here to enter year	

References

American Conference of Industrial Hygienists (ACGIH®) (2018) TLVs® and BEIs® with 7th Edition Documentation, CD-ROM, Single User Version. Copyright 2018. Reprinted with permission. See the *TLVs® and BEIs® Guidelines section* on the ACGIH website.

Deutsche Forschungsgemeinschaft (DFG) (1999) Chlorobenzene – MAK value documentation.

EU Scientific Committee on Occupational Exposure Limits (SCOEL) (2003) Recommendation from the Scientific Committee on Occupational Exposure Limits for monochlorobenzene. SCOEL/SUM/42.

European Chemicals Agency (ECHA) (2013) Chlorobenzene – REACH assessment.

National Industrial Chemicals Notification and Assessment Scheme (NICNAS) (2016) Chlorobenzene: Human health tier II assessment – IMAP report.

UK Health and Safety Executive (HSE) (2008) Chlorobenzene – EH64: Summary criteria for occupational exposure limits.

US National Institute for Occupational Safety and Health (NIOSH) (1994) Immediately dangerous to life or health concentrations – Chlorobenzene.