

CHLORINE

CAS number: 7782-50-5

Synonyms: Bertholite, chlorr, cloro, chlorine gas

Chemical formula: Cl₂

Structural formula:

Workplace exposure standard (amended)

TWA: 0.1 ppm (0.29 mg/m³)

STEL: —

Peak limitation: 0.4 ppm (1.16 mg/m³)

Notations: —

IDLH: 10 ppm (30 mg/m³)

Sampling and analysis: The recommended value is quantifiable through available sampling and analysis techniques.

Recommendation and basis for workplace exposure standard

A TWA of 0.1 ppm (0.29 mg/m³) is recommended to protect for eye and respiratory tract irritation in exposed workers.

A peak limitation of 0.4 ppm (1.16 mg/m³) is recommended to protect for irreversible pulmonary damage.

Discussion and conclusions

Chlorine is a gas under standard conditions that hydrolyses readily. It is used in various chemical manufacturing applications. Complex mixtures of chlorine and chlorinated by-products arise from its use in disinfectant applications (ACGIH, 2018).

The critical effects of exposure are eye and respiratory tract irritation and, at higher concentrations, irreversible impairment of lung function.

The recommended TWA is derived from a LOAEL of 0.4 ppm for nasal tissue damage in rats chronically exposed by inhalation. An overall factor of 4 is applied to account for translation from a six hour per day study to an eight hour shift and for uncertainty in estimating a corresponding NOAEL.

The peak limitation is derived from a NOAEL of 0.4 ppm for lung function impairment reported for volunteers affected by airway hypersensitivity (AHR) with a corresponding LOAEL of 1 ppm (ACGIH, 2018; DFG, 2014). The peak limitation is expected to be protective for irreversible lung damage particularly in susceptible individuals.

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.

There are insufficient data available to recommend a skin notation.

DRAFT

APPENDIX

Primary sources with reports

Source	Year set	Standard
SWA	Year	Peak limitation: 1 ppm (3 mg/m³)
ACGIH	2018	TLV-TWA: 0.1 ppm (0.29 mg/m³); TLV-STEL: 0.4 ppm (1.16 mg/m³)
<p>TLV-TWA intended to minimise irritation to eyes and respiratory tract. TLV-STEL intended to minimise potential for lung oedema, restrictive lung disease and airway hyper-responsiveness.</p> <p>Summary of data:</p> <p>Severity of symptoms and extent of lung injuries depend on intensity of exposure. Inflammation of eyes and respiratory tract generally reverse within 48 h; hyper-responsiveness may be irreversible.</p> <p>TLV-TWA based on a LOAEL of 0.4 ppm for mild irritation from a chronic inhalation study (rats, 6 h/d, 5 d/wk, 2 yr) adjusted for an 8 h exposure. TLV-STEL is based on a NOAEL of 0.4 ppm for pulmonary function changes in volunteers with AHR (n=10, 1 h).</p> <p>Toxicity occurs primarily through reaction with biomolecules; hydrolysis forms mainly hypochlorous acid (HOCl), which contributes to toxicity only when antioxidant biomolecules are depleted.</p> <p>Human data:</p> <ul style="list-style-type: none"> Results from an inhalational study in human volunteers reported NOAEL of 0.4 ppm and LOAEL of 1 ppm for pulmonary function (n=10, 5 each with/without AHR, 20 L/min, 60 min). <ul style="list-style-type: none"> significant decrease in FEV in all volunteers significantly greater decrease in volunteers with AHR Workers (n=287) presented upper respiratory irritation (78%) for 5–10 d after repeat acute exposures (24–25 over 3–6 mo), 58% of which were between 0.5–8 ppm <ul style="list-style-type: none"> systemic effects reported including flu-like symptoms, fatigue, sleeping difficulties, lasting 1–3 wk post-exposure follow-up spirometry studies up to 36 mo post-exposure show that exposure can lead to persistent airflow obstruction and AHR Case study reported decreased pulmonary function in exposed (n=54) chloralkaline plant workers compared with non-exposed (n=38) workers Case studies relating chlorine exposure, e.g. from disinfectants in swimming pools, with incidences of asthma or colon/rectal cancer not considered in the evaluation due to mixed exposures and unknown relevance to chlorine-exposed workers <ul style="list-style-type: none"> positive correlation with colon cancer incidence in men noted for such chlorinated disinfection by-products. <p>Animal data:</p> <ul style="list-style-type: none"> AHR induced with methacholine in mice exposed at 400 ppm for 5 min 1–3 d post-exposure Impaired antimicrobial activity in lungs of mice following 400 ppm exposure for 30 min Induced lung oedema, airway inflammation and AHR in mice at 50 or 200 ppm (15 min) <ul style="list-style-type: none"> low exposure group presented symptoms after 6 h; high exposure group after 12 h inflammatory responses reversed after 48 h, AHR sustained for at least 28 d Effects of exposure depend non-linearly on time and concentration (mice, 100 ppm/h): <ul style="list-style-type: none"> 0% survival at 800 ppm/7.5 min 100% survival at 200 ppm/30 min and 100 ppm/60 min lung injury most pronounced at 400 ppm/15 min 		

Source	Year set	Standard
<ul style="list-style-type: none"> • LOAEL: 0.4 ppm for respiratory tract lesions/degeneration (mice and male rats, 6 h/d, 5 d/wk, 2 yr) (female rats, 3 alternate d/wk, 2 yr) <ul style="list-style-type: none"> ◦ male mice and female rats more sensitive to chlorine than female mice and male rats ◦ positive concentration dependence for lesion incidence and severity • LOAEL: 2.3 ppm for upper respiratory tract irritation (rhesus monkeys, 6 h/d, 5 d/wk, 1 yr) <ul style="list-style-type: none"> ◦ clinically non-significant changes in 0.1–0.5 ppm exposure groups. ◦ noted that these groups were likely exposed to 0 or 0.23±0.15 ppm, respectively, due to losses from reaction of chlorine with ammonia in the test environment • <i>In vitro</i> studies hampered by chlorine hydrolysis. However, some chlorinated biomolecules are genotoxic/carcinogenic, mixtures of which can be generated upon absorption. 		
DFG	2004	MAK: 0.5 ppm (1.5 mg/m³)
<p>Summary of additional data:</p> <p>MAK dates from 1961 and is retained based on evidence from animal and human studies that do not indicate it should be lowered. No data available for sensitising effects or dermal absorption.</p> <p>Human data:</p> <ul style="list-style-type: none"> • Acute bronchial inflammation at 66 ppm reported in case study of accidental release (<1 h, no further information provided) • Subjective eye and respiratory tract irritation without lung function impairment noted at 1 ppm (n=8, 2 h), significant irritation occurs at 2 ppm (n=8, 2 h) • Reduced lung function in exposed non-smoking workers at pulp mill at 0.18 ppm (n=4, 8.9±8.6 yr) • Case study of 15 pregnancies in chlorine plant workers exposed at 0.9–1.7 ppm (6 h/d, unknown duration) reported 2 stillbirths, concluded that exposure had no reproductive toxicity (no further information provided) • Non-mutagenic in male workers exposed at <1 ppm for 10.9 yr (average) • No inflammatory effect to nose or changes in lung function at 0.5 ppm (n=8, 3 h/d, 2 times/d, 3 d). <p>Animal data:</p> <ul style="list-style-type: none"> • LOAEL of 0.4 ppm in long-term rat exposure study cited by ACGIH, 2018 questioned due to confounding exposure to chloramine in test environment • LC₅₀: 123–630 ppm (mice, 30 min), 600 ppm (dogs, 30 min) • Bacterial <i>in vitro</i> study (using gas, unclear if closed system) reported cytotoxicity at 25 ppm but no mutagenicity • Other <i>in vitro</i> studies using sodium hypochlorite inconclusive due to cytotoxicity and alkalinity of reagent • Respiratory rate depression 50% (RD₅₀): 9.3 ppm (mice, 10 min), 3.5 ppm (mice, 1 h). 		
SCOEL	1998	15-minute TWA: 0.5 ppm (1.5 mg/m³)
<p>Summary of additional data:</p> <p>STEL of 0.5 ppm is recommended because critical effects are concentration-dependent; not time-dependent. STEL value derived from acute and chronic exposure studies in humans and rhesus monkeys, both suggest a NOAEL of 0.5 ppm.</p> <p>No information on dermal absorption of chlorine; dermal uptake considered to be very low due to rapid hydrolysis/reaction with biomolecules.</p> <p>Human data:</p> <ul style="list-style-type: none"> • Irritation and transient lung function impairment at 1 ppm (4–8 h) in acute inhalational study <ul style="list-style-type: none"> ◦ no effects noted at 0.5 ppm (8 h). 		

Source	Year set	Standard
Animal data:		
<ul style="list-style-type: none"> • LC₅₀: 293–473 ppm (rats, 1 h), 137 ppm (mice, 1 h) • LOAEL: 1 ppm for upper respiratory tract irritation and inflammation (6 h/d, 5 d/wk, 6 wk) <ul style="list-style-type: none"> ○ kidney and liver degeneration observed in 3 ppm exposure group ○ some deaths reported in 9 ppm exposure group • Follow-up tissue comparisons of mice, rats and rhesus monkeys from chronic inhalation studies showed that airflow in respiratory tract played major role in exposure-related lesion distribution <ul style="list-style-type: none"> ○ rhesus monkeys are the best model for human exposure. 		
OARS/AIHA	NA	NA
No report.		
HCOTN	NA	NA
No report.		

Secondary source reports relied upon

Source	Year	Additional information
NICNAS	✓ 2016	<ul style="list-style-type: none"> • No deaths in 19 people exposed to >1,000 ppm in a railroad car accident • Light-headedness and sore throats at 2 ppm in 2 accidentally exposed chemical plant workers (unknown duration) • Death caused by pulmonary oedema 3 h post-exposure following 30 min in gas cylinder accident.
US EPA	✓ 1994	<ul style="list-style-type: none"> • RfD calculation based on lowest NOAEL from repeat feeding study: 14.4 mg/kg/d (n=70, female rats, daily, 2 yr) • Inhalational data not presented.
OECD	✓ 2003	<ul style="list-style-type: none"> • 15 min TWA of 0.5 ppm recommended • Inconclusive mutagenicity <i>in vitro</i> due to hypochlorite formation, non-genotoxic <i>in vivo</i> however due to cytotoxicity • No evidence for carcinogenicity in humans.
US NIOSH	✓ 1994	<ul style="list-style-type: none"> • The revised IDLH for chlorine is 10 ppm based on acute inhalation toxicity data in humans.

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	—
HCIS	—

Source	Notations
NICNAS	—
EU Annex	—
ECHA	NA
ACGIH	Carcinogenicity – A4
DFG	—
SCOEL	—
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

Insufficient data to assign a skin notation.

IDLH

Is there a suitable IDLH value available? Yes

Additional information

Molecular weight:	70.91
Conversion factors at 25°C and 101.3 kPa:	1 ppm = Number mg/m ³ ; 1 mg/m ³ = Number ppm
This chemical is used as a pesticide:	✓
This chemical is a biological product:	<input type="checkbox"/>
This chemical is a by-product of a process:	✓
A biological exposure index has been recommended by these agencies:	<input type="checkbox"/> ACGIH <input type="checkbox"/> DFG <input type="checkbox"/> 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) (2004) Chlorine – MAK value documentation.

EU Scientific Committee on Occupational Exposure Limits (SCOEL) (1998) Recommendation from the Scientific Committee on Occupational Exposure Limits for chlorine. SCOEL/SUM/76.

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

Organisation for Economic Cooperation and Development (OECD) (2003) SIDS initial assessment profile – Chlorine.

US Environmental Protection Agency (US EPA) (1994) Chlorine; CASRN 7782-50-5 – IRIS documentation.

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